08/244863

PATENT
Attorney Docket No. 20006 US

I hereby certify that this correspondence is being filed with the United States Patent and Trademark Office to the Commissioner for Patents via hand delivery to Office of Patent Legal Administration, Room MDW 7D55, 600 Dulany Street (Madison Building), Alexandria, VA 22314 on this ___ day of February 2009.

By _____
(Signature of person delivering)

_____
(Typed or printed name of person)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the patent of: Gary J. Bridger, *et al.*	Approved Product: MOZOBIL™ (plerixafor)
Patent No.: 5,583,131	U.S. F.D.A. Approval Date: December 15, 2008
Granted: December 10, 1996	
Title: AROMATIC-LINKED POLYAMINE MACROCYCLIC COMPOUNDS WITH ANTI-HIV ACTIVITY	

RECEIVED
FEB 6 2009
PATENT EXTENSION
OPLA

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C § 156

Sir:

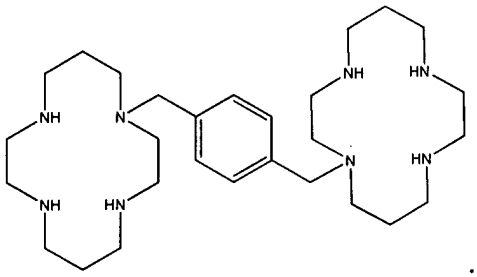
Genzyme Corporation hereby requests an extension of the patent term of the above-identified patent under 35 U.S.C. § 156. The instant request for patent term extension is timely because it is being submitted within the sixty-day period beginning on the date the product received permission under the provision of law under which the applicable regulatory review period occurred for commercial marketing or use. 35 U.S.C. § 156(d)(1). Applicants represent that Genzyme Corporation is empowered to request the instant patent term extension because Genzyme Corporation is the sole owner of the instant patent, as evidenced by the assignments recorded at: (i)

03/20/2009 RLOGAN 00000001 060916 08244863
01 FC:1457 1120.00 DA

Reel 020518 and Frame 0053 on February 15, 2008 from AnorMED Corporation to Genzyme Corporation; (ii) Reel 009638 and Frame 0749 on December 17, 1998 from Johnson Matthey Public Limited Company to AnorMED Inc.; and (iii) Reel 007684 and Frame 0045 on September 25, 1995 from inventors Gary James Bridger, Sreenivasan Padmanabhan, Ranato [*sic*] Tony Skerlj, and David Michael Thornton to Johnson Matthey Public Limited Company. By the Power of Attorney submitted herewith at Exhibit A, Applicants hereby appoint attorneys Nicole L. M. Valtz, Robert J. Bajefsky, Charles E. Van Horn and all registered practitioners associated with Customer Number 22852 at Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., as attorneys with regard to this application for extension of the term of U.S. Patent No. 5,583,131.

Applicants hereby submit this application for extension of the patent term under 35 U.S.C. § 156 by providing the following information required by the rules promulgated by the U.S. Patent and Trademark Office (37 C.F.R. § 1.740). For the convenience of the Patent and Trademark Office, the information contained in this application is presented in a format which follows the requirements of Section 1.740 of Title 37 of the Code of Federal Regulations.

(1) The approved product, MOZOBIL™ (plerixafor), is a small molecule. The chemical name of plerixafor is 1,1'-[1,4-phenylenebis(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane. The chemical structure of plerixafor is:



(2) The approved product, MOZOBIL™ (plerixafor), was subject to regulatory review under the Federal Food, Drug and Cosmetic Act, Section 505, Part (b)(1).

(3) The approved product, MOZOBIL™ (plerixafor), received permission for commercial marketing or use under Section 505, Part (b)(1) of the Federal Food, Drug and Cosmetic Act on December 15, 2008.

(4) The active ingredient in MOZOBIL™ is plerixafor, which on information and belief, has not been approved for commercial marketing or use under Section 505 of the Federal Food, Drug, and Cosmetic Act prior to the approval of NDA 22-311 for MOZOBIL™ by the Food and Drug Administration on December 15, 2008. A copy of the package insert describing the approved product is attached (Exhibit B).

(5) This application for extension of patent term under 35 U.S.C. § 156 is being submitted within the permitted sixty-day period pursuant to 37 C.F.R. § 1.720(f), said period will expire on February 12, 2009, if December 15, 2008, is day one (1) of the sixty (60) day period.

(6) The complete identification of the patent for which a term extension is being sought is as follows:

Inventors:	Gary J. Bridger; Sreenivasan Padmanbhan [*sic*]; Renato T. Skerlj; David M. Thornton
Patent No.:	5,583,131
Issue Date:	December 10, 1996
Expiration Date:	December 10, 2013 (by virtue of the patent term resetting provisions of 35 U.S.C. § 154(c)(1) enacted under the Uruguay Round Agreements Act).

(7) A true and complete copy of the patent for which an extension is being sought is attached at Exhibit C.

(8) No terminal disclaimer, reexamination certificate, or certificate of correction has been issued on this patent. A copy of: (i) the maintenance fee statement indicating payment of the twelve-year maintenance fee on June 10, 2008; and (ii) the patent bibliographic information indicating payment of the fee deficiency under 37 C.F.R. § 1.28(c) on January 22, 2009 are attached at Exhibit D.

(9) Claims 1 and 2 of U.S. Patent No. 5,583,131 claim a pharmaceutical composition comprising the active ingredient of MOZOBIL™.

Claim 1 reads as follows:

1. A pharmaceutical composition active against HIV comprising as an active ingredient a linked cyclic compound of formula I,

Z-R-A-R'-Y (I)

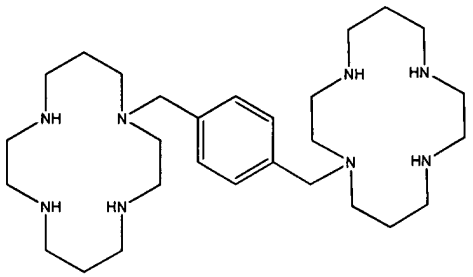
in which Z and Y are identical cyclic polyamine moieties having from 10 to 15 ring members and from 3 to 6 amine nitrogens in the ring spaced by 2 or more carbon atoms from each other, said amine nitrogens being the only ring heteroatoms,

A is an aromatic or heteroaromatic moiety other than quinoline,

R and R' are each methylene linked to nitrogen atoms in Z and Y,

the amine nitrogen atoms being otherwise unsubstituted.

Claim 1 claims the approved product because it claims a pharmaceutical composition that comprises a genus of compounds of formula I that embraces the active ingredient of MOZOBIL™, which is plerixafor. The chemical structure of plerixafor is reproduced here for the convenience of the Office:



It is apparent from the chemical structure of plerixafor that with reference to formula I in claim 1: (i) Z and Y are identical cyclic polyamine moieties having from 10 to 15 ring members and from 3 to 6 amine nitrogens in the ring spaced by 2 or more carbon atoms from each other, said amine nitrogens being the only ring heteroatoms; (ii) A is an aromatic moiety; and (iii) R and R' are each methylene linked to nitrogen atoms in Z and Y, the amine nitrogen atoms being otherwise unsubstituted.

Claim 2 reads as follows:

2. A composition according to claim 1, wherein in the compound of formula I, each moiety Z and Y has 14 ring members and 4 amine nitrogens in the ring.

It is apparent from the chemical structure of plerixafor that with reference to formula I in claim 1, from which claim 2 directly depends, each moiety Z and Y has 14 ring members and 4 amine nitrogens in the ring.

[REMAINDER OF PAGE INTENTIONALLY BLANK]

(10) The relevant dates and information pursuant to 35 U.S.C. § 156(g) to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

Investigational New Drug Application (IND 55,851) for MOZOBIL™ was submitted on May 4, 1998 and became effective on June 3, 1998.

New Drug Application (NDA 022-311) for MOZOBIL™ was submitted on June 16, 2008.

New Drug Application (NDA 022-311) for MOZOBIL™ was approved on December 15, 2008.

[REMAINDER OF PAGE INTENTIONALLY BLANK]

(11) A brief description of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect MOZOBIL™ and the dates applicable to these significant activities are set forth in a chronology of events at Exhibit E.

[REMAINDER OF PAGE INTENTIONALLY BLANK]

(12)(i) U.S. Patent No. 5,583,131 is eligible for extension of the patent term under 35 U.S.C. § 156 because it satisfies all of its requirements for such extension. For the convenience of the Patent and Trademark Office, the requirements for extension of a patent term under 35 U.S.C. § 156 are presented in a format which follows Section 156 of Title 35 of the United States Code.

(a) 35 U.S.C. § 156 - U.S. Patent No. 5,583,131 claims the product MOZOBIL™.

(b) 35 U.S.C. § 156(a)(1) - U.S. Patent No. 5,583,131 has not expired before submission of the instant application.

(c) 35 U.S.C. § 156(a)(2) - The term of U.S. Patent No. 5,583,131 has never been extended under 35 U.S.C. § 156(e)(1).

(d) 35 U.S.C. § 156(a)(3) - The application for extension is submitted by the owner of record of the patent in accordance with the requirements of paragraphs (1) through (4) of 35 U.S.C. § 156(d) and the rules of the Patent and Trademark Office.

(e) 35 U.S.C. § 156(a)(4) - The product MOZOBIL™ has been subject to a regulatory review period before its commercial marketing or use.

(f) 35 U.S.C. § 156(a)(5)(A) - the permission for the commercial marketing or use of the product MOZOBIL™ after the regulatory review period is the first permitted commercial marketing or use of the product MOZOBIL™ under the provision of the Federal Food, Drug and Cosmetic Act (i.e., Section 505) under which such regulatory review period occurred.

(g) 35 U.S.C. § 156(c)(4) - No other patent has been extended under 35 U.S.C. § 156(e)(i) for the same regulatory review period for any product, including the product MOZOBIL™.

(12)(ii) The length of the extension of patent term of U.S. Patent No. 5,583,131 claimed by Applicants is that period authorized by 35 U.S.C. § 156(c), which has been calculated to be 1,826 days (or 5 years). The length of the extension was determined pursuant to Section 1.775 of Title 37 of the Code of Federal Regulations as follows:

(a) The length of the regulatory review period under 37 C.F.R. § 1.775(c) is calculated as beginning on June 3, 1998 and ending on December 15, 2008, which is a total of 3,849 days, which is the sum of (1) and (2) below:

(1) The number of days in the "Testing Phase" under 35 U.S.C. § 156(g)(1)(B)(i), which is calculated to be 3,666 days, which is the period beginning on the date an exemption under subsection (i) of Section 505 of the Federal Food, Drug, and Cosmetic Act became effective for the approved product MOZOBIL™, which is June 3, 1998, and ending on the date an application was initially submitted for the product MOZOBIL™ under such section, which is June 16, 2008; and

(2) The number of days in the "Approval Phase" under 35 U.S.C. § 156(g)(1)(B)(ii), which is calculated to be 183 days, which is the number of days in the period beginning on the date the application the application was initially submitted for the approved product MOZOBIL™ under subsection (b) of Section 505 of the Federal Food, Drug, and Cosmetic Act, which is June 16, 2008, and ending on the date such application was approved under such section, which is December 15, 2008.

(b) The term of the patent as extended is determined by:

(1) Subtracting from the length of the regulatory review period under 37 C.F.R. § 1.775(c) calculated according to sub-paragraph (12)(ii)(a) above (3,849 days), the sum of the periods (A) to (C) below, which is calculated to be 1,833 days, to arrive at a period of 2,016 days:

(A) The number of days in the regulatory review period which were on and before the date on which the patent issued (December 10, 1996), which is zero (0) days; and

(B) The number of days in the regulatory review period during which applicant did not act with due diligence, which is zero (0) days; and

(C) One-half the number of days remaining in the regulatory review period determined in sub-paragraph (12)(ii)(a)(1) (i.e., the Testing Phase) after that period is reduced in accordance with the determinations of sub-paragraphs (12)(ii)(b)(1)(A) and (12)(ii)(b)(1)(B) immediately above ignoring any half-days (one-half of 3,666 days), which is 1,833 days; and

(2) Adding the number of days determined in sub-paragraph (12)(ii)(a)(2), which is 183 days, to the original term of the patent as shortened by any terminal disclaimer, to arrive at a period of 2,199 days (i.e., the sum of 2,016 days and 183 days),

(c) The number of days as determined in sub-paragraph (12)(ii)(b) (2,199 days) when added to the expiration date of the original term of the U.S. Patent No. 5,583,131 (December 10, 2013) would result in the date of December 18, 2019.

(d) Adding fourteen (14) years to the date of approval of the application under subsection (b) of section 505 of the Federal Food, Drug, and Cosmetic Act (December 15, 2008) is determined to be December 15, 2022.

(e) Comparing the date for the end of the period obtained pursuant to sub-paragraph (12)(ii)(c), which is to December 18, 2019, with the date for the end of the period obtained pursuant to sub-paragraph (12)(ii)(d), which is December 15, 2022, the earlier date of December 18, 2019 is selected.

(f) Because U.S. Patent No. 5,583,131 was issued after September 24, 1984, the dates under sub-paragraphs (12)(f)(1) and (12)(f)(2) are determined:

(1) the date obtained by adding five (5) years to the original expiration date of the U.S. Patent No. 5,583,131 as shortened by any terminal disclaimer, which is December 10, 2018; and

(2) the date obtained in sub-paragraph (12)(ii)(e), which is December 18, 2019.

(g) Comparing the date determined under sub-paragraph (12)(ii)(f)(1) and (12)(ii)(f)(2) and selecting the earlier date results in a selection of December 10, 2018.

(h) In summary, Applicant's calculation of the extension of the patent term under 35 U.S.C. § 156 for U.S. Patent No. 5,583,131 results in a period of extension of 5 years (1,826 days), thereby extending the patent term from December 10, 2013 to December 10, 2018.

(13) Applicants acknowledge a duty to disclose to the Director of the United States Patent and Trademark Office and the Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension sought.

(14) The Commissioner is hereby authorized by this paper to charge the required fee of $1,120.00 under 37 C.F.R. § 1.20(j)(1) or any additional amount due or credit any overpayment to Deposit Account 06-0916.

(15) All correspondence and inquiries may be directed to the undersigned, whose address, telephone number, and fax number are as follows:

Charles E. Van Horn

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

901 New York Avenue, N.W.

Washington, D.C. 20001-4413

Phone: 202-408-4000

Fax: 202-408-4400

Customer Number 22852

[REMAINDER OF PAGE INTENTIONALLY BLANK]

(16) Applicants hereby certify that the instant application for extension of patent term under 35 U.S.C. § 156 including all Exhibits and supporting papers is being submitted as one original and two (2) additional copies thereof at Exhibit F pursuant to 37 C.F.R. § 1.740(b).

Respectfully submitted,

Date: 06 February 2009

Charles E. Van Horn

Charles E. Van Horn
Attorney for Applicants
Reg. No. 40,266

Customer No. 22852
Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
901 New York Avenue, N.W.
Washington, D.C. 20001-4413
Phone: 202-408-4000

List of Attachments:

Power of Attorney (Exhibit A)
Package Insert for MOZOBIL™ (plerixafor) (Exhibit B)
U.S. Patent No. 5,583,131 (Exhibit C)
Copy of Maintenance Fee Statement and Patent Bibliographic Information (Exhibit D)
Chronology of Regulatory Review Period (Exhibit E)
Certification of Copies of Application Papers and two (2) additional copies (Exhibit F)

EXHIBIT A

In re patent of Gary J. Bridger et al.
USP 5,583,131
Approved Product: MOZOBIL™ (plerixafor)
Application for Patent Term Extension
Customer No. 22852

PATENT
Attorney Docket No. 20006 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the patent of: Gary J. Bridger, *et al.*	)	Approved Product: MOZOBIL™ (plerixafor)	
Patent No.: 5,583,131	)	U.S. F.D.A. Approval Date: December 15, 2008	
Granted: December 10, 1996	)		
Title: AROMATIC-LINKED POLYAMINE MACROCYCLIC COMPOUNDS WITH ANTI-HIV ACTIVITY	)		

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

GRANT OF POWER OF ATTORNEY BY ASSIGNEE AND STATEMENT UNDER 37 C.F.R. § 3.73(b)

Sir:

The undersigned authorized representative of the assignee hereby grants its power of attorney to practitioners associated with **FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P., Customer Number 22,852,** including Robert D. Bajefsky, Reg. No. 25,387; Charles E. Van Horn, Reg. No. 40,266; and Nicole L. M. Valtz, Reg. No. 47,150, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith. Pursuant to 37 C.F.R. § 3.73(b) the undersigned states that the assignee of record for this application is Genzyme Corporation, as evidenced by a chain of title from the inventor(s), of the patent identified above, to the current assignee as shown below:

1. From: Gary James Bridger, Sreenivasan Padmanabhan, Renato Tony Skerlj, and David Michael Thornton To: Johnson Matthey Public Limited Company.
The document was recorded in the Patent and Trademark Office on September 25, 1995 at Reel 007684, Frame 0045, or a copy is attached.

2. From: Johnson Matthey Public Limited Company To: AnorMED Inc.
The document was recorded in the Patent and Trademark Office on December 17, 1998 at Reel 009638, Frame 0749, or a copy is attached.

3. From: AnorMED Corporation To: Genzyme Corporation.
The document was recorded in the Patent and Trademark Office on February 15, 2008 at Reel 020518, Frame 0053, or a copy is attached.

Please send all future correspondence concerning this application to Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., Customer No. 22,852.

Date: Jan 29, 2009 By: M.K. Shafmaster

Madge K. Shafmaster
Senior Vice President, Chief Patent Counsel
Genzyme Corporation

EXHIBIT B

In re patent of Gary J. Bridger et al.
USP 5,583,131
Approved Product: MOZOBIL™ (plerixafor)
Application for Patent Term Extension
Customer No. 22852

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MOZOBIL safely and effectively. See full prescribing information for MOZOBIL.

MOZOBIL (plerixafor injection), Solution for Subcutaneous use
Initial U.S. Approval: 2008

INDICATIONS AND USAGE

Mozobil, a hematopoietic stem cell mobilizer, is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma. (1)

DOSAGE AND ADMINISTRATION

- Initiate Mozobil treatment after the patient has received G-CSF once daily for 4 days. (2.1)
- Repeat Mozobil dose up to 4 consecutive days. (2.1)
- Select dose based on 0.24 mg/kg actual body weight. (2.1)
- Administer by subcutaneous injection approximately 11 hours prior to initiation of apheresis. (2.1)
- Renal impairment: If creatinine clearance is ≤ 50 mL/min, decrease dose by one-third to 0.16 mg/kg. (2.3)

DOSAGE FORMS AND STRENGTHS

- Single-use vial containing 1.2 mL of a 20 mg/mL solution. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Tumor Cell Mobilization in Leukemia Patients: Mozobil may mobilize leukemic cells and should not be used in leukemia patients (5.1)
- Hematologic Effects: Increased circulating leukocytes and decreased platelet counts have been observed. Monitor blood cell counts and platelet counts during Mozobil use. (5.2)
- Potential for Tumor Cell Mobilization: Tumor cells may be released from marrow during HSC mobilization with Mozobil and G-CSF. Effect of reinfusion of tumor cells is unknown. (5.3)
- Potential for Splenic Rupture: Evaluate patients who report left upper abdominal and/or scapular or shoulder pain. (5.4)
- Pregnancy: May cause fetal harm. Advise women not to become pregnant when taking Mozobil. (5.5, 8.1)

ADVERSE REACTIONS

Most common adverse reactions (≥ 10%): diarrhea, nausea, fatigue, injection site reactions, headache, arthralgia, dizziness, and vomiting. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-877-4MOZOBIL or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See 17 for PATIENT COUNSELING INFORMATION

Revised: 12/2008

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Mozobil™ (plerixafor injection) is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage and Administration

Vials should be inspected visually for particulate matter and discoloration prior to administration and should not be used if there is particulate matter or if the solution is discolored.

Begin treatment with Mozobil after the patient has received G-CSF once daily for four days. *[see Dosage and Administration (2.2)]* Administer Mozobil approximately 11 hours prior to initiation of apheresis for up to 4 consecutive days.

The recommended dose of Mozobil is 0.24 mg/kg body weight by subcutaneous (SC) injection. Use the patient's actual body weight to calculate the volume of Mozobil to be administered. Each vial delivers 1.2 mL of 20 mg/mL solution, and the volume to be administered to patients should be calculated from the following equation:

0.012 X patient's actual body weight (in kg) = volume to be administered (in mL)

In clinical studies, Mozobil dose has been calculated based on actual body weight in patients up to 175% of ideal body weight. Mozobil dose and treatment of patients weighing more than 175% of ideal body weight have not been investigated.

Based on increasing exposure with increasing body weight, the plerixafor dose should not exceed 40 mg/day. *[see Clinical Pharmacology (12.3)]*

2.2 Recommended Concomitant Medications

Administer daily morning doses of G-CSF 10 micrograms/kg for 4 days prior to the first evening dose of Mozobil and on each day prior to apheresis. *[see Clinical Studies (14)]*

2.3 Dosing in Renal Impairment

In patients with moderate and severe renal impairment (estimated creatinine clearance (CL_{CR}) ≤ 50 mL/min), reduce the dose of Mozobil by one-third to 0.16 mg/kg as shown in Table 1. If CL_{CR} is ≤ 50 mL/min the dose should not exceed 27 mg/day, as the mg/kg-based dosage results in increased plerixafor exposure with increasing body weight. *[see Clinical Pharmacology (12.3)]* Similar systemic exposure is predicted if the dose is reduced by one-third in patients with moderate and severe renal impairment compared with subjects with normal renal function. *[see Clinical Pharmacology (12.3)]*

Table 1: Recommended Dosage of Plerixafor in Patients with Renal Impairment

Estimated Creatinine Clearance (mL/min)	Dose
> 50	0.24 mg/kg once daily (not to exceed 40 mg/day)
≤ 50	0.16 mg/kg once daily (not to exceed 27 mg/day)

The following (Cockroft-Gault) formula may be used to estimate CL_{CR}:

Males:

$$\text{Creatinine clearance (mL/min)} = \frac{\text{weight (kg)} \times (140 - \text{age in years})}{72 \times \text{serum creatinine (mg/dL)}}$$

Females:

Creatinine clearance (mL/min) = 0.85 X value calculated for males

There is insufficient information to make dosage recommendations in patients on hemodialysis.

3 DOSAGE FORMS AND STRENGTHS

Single-use vial containing 1.2 mL of a 20 mg/mL solution.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Tumor Cell Mobilization in Leukemia Patients

For the purpose of HSC mobilization, Mozobil may cause mobilization of leukemic cells and subsequent contamination of the apheresis product. Therefore, Mozobil is not intended for HSC mobilization and harvest in patients with leukemia.

5.2 Hematologic Effects

Leukocytosis

Administration of Mozobil in conjunction with G-CSF increases circulating leukocytes as well as HSC populations. Monitor white blood cell counts during Mozobil use. Exercise clinical judgment when administering Mozobil to patients with peripheral blood neutrophil counts above 50,000/mcL.

Thrombocytopenia

Thrombocytopenia has been observed in patients receiving Mozobil. Monitor platelet counts in all patients who receive Mozobil and then undergo apheresis.

5.3 Potential for Tumor Cell Mobilization

When Mozobil is used in combination with G-CSF for HSC mobilization, tumor cells may be released from the marrow and subsequently collected in the leukapheresis product. The effect of potential reinfusion of tumor cells has not been well-studied.

5.4 Splenic Enlargement and Potential for Rupture

Higher absolute and relative spleen weights associated with extramedullary hematopoiesis were observed following prolonged (2 to 4 weeks) daily plerixafor SC administration in rats at doses approximately 4-fold higher than the recommended human dose based on body surface area. The effect of Mozobil on spleen size in patients was not specifically evaluated in clinical studies. Evaluate individuals receiving Mozobil in combination with G-CSF who report left upper abdominal pain and/or scapular or shoulder pain for splenic integrity.

5.5 Pregnancy

Pregnancy Category D

Mozobil may cause fetal harm when administered to a pregnant woman. Plerixafor was teratogenic in animals. There are no adequate and well-controlled studies in pregnant women using Mozobil. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with Mozobil. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. *[see Use In Specific Populations (8.1)]*

6 ADVERSE REACTIONS

6.1 Clinical Trial Experience

The following serious adverse reactions are discussed elsewhere in the labeling:

- Potential for tumor cell mobilization in leukemia patients *[see Warnings and Precautions (5.1)]*
- Increased circulating leukocytes and decreased platelet counts *[see Warnings and Precautions (5.2)]*
- Potential for splenic enlargement *[see Warnings and Precautions (5.4)]*

The most common adverse reactions (≥ 10%) reported in patients who received Mozobil in conjunction with G-CSF regardless of causality and more frequent with Mozobil than placebo during HSC mobilization and apheresis were diarrhea, nausea, fatigue, injection site reactions, headache, arthralgia, dizziness, and vomiting.

Safety data for Mozobil in combination with G-CSF were obtained from two placebo-controlled studies and 10 uncontrolled studies in 543 patients. Patients were primarily treated with Mozobil at daily doses of 0.24 mg/kg SC. Median exposure to Mozobil in these studies was 2 days (range 1 to 7 days).

In the two randomized studies in patients with NHL and MM, a total of 301 patients were treated in the Mozobil and G-CSF group and 292 patients were treated in the placebo and G-CSF group. Patients received daily morning doses of G-CSF 10 micrograms/kg for 4 days prior to the first dose of Mozobil 0.24 mg/kg SC or placebo and on each morning prior to apheresis. The adverse reactions that occurred in ≥ 5% of the patients who received Mozobil regardless of causality and were more frequent with Mozobil than placebo during HSC mobilization and apheresis are shown in Table 2.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Table 2: Adverse Reactions in ≥ 5% of Non-Hodgkin's Lymphoma and Multiple Myeloma Patients Receiving Mozobil and More Frequent than Placebo During HSC Mobilization and Apheresis

	Percent of Patients (%)					
	Mozobil and G-CSF (n = 301)			Placebo and G-CSF (n = 292)		
	All Grades[a]	Grade 3	Grade 4	All Grades	Grade 3	Grade 4
Gastrointestinal disorders						
Diarrhea	37	< 1	0	17	0	0
Nausea	34	1	0	22	0	0
Vomiting	10	< 1	0	6	0	0
Flatulence	7	0	0	3	0	0
General disorders and administration site conditions						
Injection site reactions	34	0	0	10	0	0
Fatigue	27	0	0	25	0	0
Musculoskeletal and connective tissue disorders						
Arthralgia	13	0	0	12	0	0
Nervous system disorders						
Headache	22	< 1	0	21	1	0
Dizziness	11	0	0	6	0	0
Psychiatric disorders						
Insomnia	7	0	0	5	0	0

[a]Grades based on criteria from the World Health Organization (WHO)

In the randomized studies, 34% of patients with NHL or MM had mild to moderate injection site reactions at the site of subcutaneous administration of Mozobil. These included erythema, hematoma, hemorrhage, induration, inflammation, irritation, pain, paresthesia, pruritus, rash, swelling, and urticaria.

Mild to moderate systemic reactions were observed in less than 1% of patients approximately 30 min after Mozobil administration. Events included one or more of the following: urticaria (n = 2), periorbital swelling (n = 2), dyspnea (n = 1) or hypoxia (n = 1). Symptoms generally responded to treatments (e.g., antihistamines, corticosteroids, hydration or supplemental oxygen) or resolved spontaneously.

Vasovagal reactions, orthostatic hypotension, and/or syncope can occur following subcutaneous injections. In Mozobil oncology and healthy volunteer clinical studies, less than 1% of subjects experienced vasovagal reactions following subcutaneous administration of Mozobil doses ≤ 0.24 mg/kg. The majority of these events occurred within 1 hour of Mozobil administration. Because of the potential for these reactions, appropriate precautions should be taken.

Other adverse reactions that occurred in < 5% of patients but were reported as related to Mozobil during HSC mobilization and apheresis included abdominal pain, hyperhidrosis, abdominal distention, dry mouth, erythema, stomach discomfort, malaise, hypoesthesia oral, constipation, dyspepsia, and musculoskeletal pain.

7 DRUG INTERACTIONS

Based on *in vitro* data, plerixafor is not a substrate, inhibitor or inducer of human cytochrome P450 isozymes. Plerixafor is not likely to be implicated in *in vivo* drug-drug interactions involving cytochrome P450s. *[see Clinical Pharmacology (12.3)]*

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category D

Plerixafor was teratogenic in animals. Plerixafor administered to pregnant rats induced embryo-fetal toxicities including fetal death, increased resorptions and post-implantation loss, decreased fetal weights, anophthalmia, shortened digits, cardiac interventricular septal defect, ringed aorta, globular heart, hydrocephaly, dilatation of olfactory ventricles, and retarded skeletal development. Embryo-fetal toxicities occurred mainly at a dose of 90 mg/m^2 (approximately 10 times the recommended human dose of 0.24 mg/kg when compared on a mg/m^2 basis or 10 times the AUC in subjects with normal renal function who received a single dose of 0.24 mg/kg).

8.3 Nursing Mothers

It is not known whether plerixafor is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from Mozobil, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

The safety and efficacy of Mozobil in pediatric patients have not been established in controlled clinical studies.

8.5 Geriatric Use

Of the total number of subjects in controlled clinical studies of Mozobil, 24% were 65 and over, while 0.8% were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Since plerixafor is mainly excreted by the kidney, no dose modifications are necessary in elderly individuals with normal renal function. In general, care should be taken in dose selection for elderly patients due to the greater frequency of decreased renal function with advanced age. Dosage adjustment in elderly patients with $CL_{CR} \leq 50$ mL/min is recommended. *[see Dosage and Administration (2.3) and Clinical Pharmacology (12.3)]*

8.6 Renal Impairment

In patients with moderate and severe renal impairment ($CL_{CR} \leq 50$ mL/min), reduce the dose of plerixafor by one-third to 0.16 mg/kg. *[see Dosage and Administration (2.3) and Clinical Pharmacology (12.3)]*

10 OVERDOSAGE

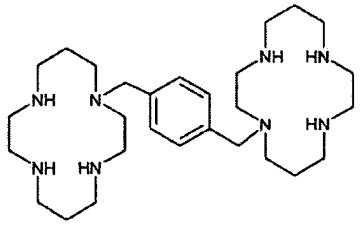
Based on limited data at doses above the recommended dose of 0.24 mg/kg SC, the frequency of gastrointestinal disorders, vasovagal reactions, orthostatic hypotension, and/or syncope may be higher.

11 DESCRIPTION

Mozobil (plerixafor injection) is a sterile, preservative-free, clear, colorless to pale yellow, isotonic solution for subcutaneous injection. Each mL of the sterile solution contains 20 mg of plerixafor. Each single-use vial is filled to deliver 1.2 mL of the sterile solution that contains 24 mg of plerixafor and 5.9 mg of sodium chloride in Water for Injection adjusted to a pH of 6.0 to 7.5 with hydrochloric acid and with sodium hydroxide, if required.

Plerixafor is a hematopoietic stem cell mobilizer with a chemical name 1, 1'-[1,4-phenylenebis (methylene)]-bis-1,4,8,11- tetraazacyclotetradecane. It has the molecular formula $C_{28}H_{54}N_8$. The molecular weight of plerixafor is 502.79 g/mol. The structural formula is provided in Figure 1.

Figure 1: Structural Formula



Plerixafor is a white to off-white crystalline solid. It is hygroscopic. Plerixafor has a typical melting point of 131.5 °C. The partition coefficient of plerixafor between 1-octanol and pH 7 aqueous buffer is < 0.1.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Plerixafor is an inhibitor of the CXCR4 chemokine receptor and blocks binding of its cognate ligand, stromal cell-derived factor-1α (SDF-1α). SDF-1α and CXCR4 are recognized to play a role in the trafficking and homing of human hematopoietic stem cells (HSCs) to the marrow compartment. Once in the marrow, stem cell CXCR4 can act to help anchor these cells to the marrow matrix, either directly via SDF-1α or through the induction of other adhesion molecules. Treatment with plerixafor resulted in leukocytosis and elevations in circulating hematopoietic progenitor cells in mice, dogs and humans.

CD34+ cells mobilized by plerixafor were capable of engraftment with long-term repopulating capacity up to one year in canine transplantation models.

12.2 Pharmacodynamics

Data on the fold increase in peripheral blood CD34+ cell count (cells/mcL) by apheresis day were evaluated in two placebo-controlled clinical studies in patients with NHL and MM (Study 1 and Study 2, respectively). The fold increase in CD34+ cell count (cells/mcL) over the 24-hour period starting from the day prior to the first apheresis and ending the next morning just before the first apheresis is summarized in Table 3. During this 24-hour period, a single dose of Mozobil or placebo was administered 10 to 11 hours prior to apheresis.

Table 3: Fold Increase in Peripheral Blood CD34+ Cell Count Following Pretreatment with G-CSF and Administration of Plerixafor

Study	Mozobil and G-CSF		Placebo and G-CSF	
	Median	Mean (SD)	Median	Mean (SD)
Study 1	5.0	6.2 (5.4)	1.4	1.9 (1.5)
Study 2	4.8	6.4 (6.8)	1.7	2.4 (7.3)

In pharmacodynamic studies of Mozobil in healthy volunteers, peak mobilization of CD34+ cells was observed between 6 and 9 hours after administration. In pharmacodynamic studies of Mozobil in conjunction with G-CSF in healthy volunteers, a sustained elevation in the peripheral blood CD34+ count was observed from 4 to 18 hours after plerixafor administration with a peak CD34+ count between 10 and 14 hours.

12.3 Pharmacokinetics

The single-dose pharmacokinetics of plerixafor 0.24 mg/kg were evaluated in patients with NHL and MM following pre-treatment with G-CSF (10 micrograms/kg once daily for 4 consecutive days). Plerixafor exhibits linear kinetics between the 0.04 mg/kg to 0.24 mg/kg dose range. The pharmacokinetics of plerixafor were similar across clinical studies in healthy subjects who received plerixafor alone and NHL and MM patients who received plerixafor in combination with G-CSF.

A population pharmacokinetic analysis incorporated plerixafor data from 63 subjects (NHL patients, MM patients, subjects with varying degrees of renal impairment, and healthy subjects) who received a single SC dose (0.04 mg/kg to 0.24 mg/kg) of plerixafor. A two-compartment disposition model with first order absorption and elimination was found to adequately describe the plerixafor concentration-time profile. Significant relationships between clearance and creatinine clearance (CL_{CR}), as well as between central volume of distribution and body weight were observed. The distribution half-life ($t_{1/2\alpha}$) was estimated to be 0.3 hours and the terminal population half-life ($t_{1/2\beta}$) was 5.3 hours in patients with normal renal function.

The population pharmacokinetic analysis showed that the mg/kg-based dosage results in an increased plerixafor exposure ($AUC_{0\text{-}24h}$) with increasing body weight. There is limited experience with the 0.24 mg/kg dose of plerixafor in patients weighing above 160 kg. Therefore the dose should not exceed that of a 160 kg patient (i.e., 40 mg/day if CL_{CR} is > 50 mL/min and 27 mg/day if CL_{CR} is ≤ 50 mL/min). *[see Dosage and Administration (2.1, 2.3)]*

Absorption
Peak plasma concentrations occurred at approximately 30 - 60 minutes after a SC dose.

Distribution
Plerixafor is bound to human plasma proteins up to 58%. The apparent volume of distribution of plerixafor in humans is 0.3 L/kg demonstrating that plerixafor is largely confined to, but not limited to, the extravascular fluid space.

Metabolism
The metabolism of plerixafor was evaluated with *in vitro* assays. Plerixafor is not metabolized as shown in assays using human liver microsomes or human primary hepatocytes and does not exhibit inhibitory activity *in vitro* towards the major drug metabolizing cytochrome P450 enzymes (1A2, 2C9, 2C19, 2D6, and 3A4/5). In *in vitro* studies with human hepatocytes, plerixafor does not induce CYP1A2, CYP2B6, or CYP3A4 enzymes. These findings suggest that plerixafor has a low potential for involvement in cytochrome P450-dependent drug-drug interactions.

Elimination
The major route of elimination of plerixafor is urinary. Following a 0.24 mg/kg dose in healthy volunteers with normal renal function, approximately 70% of the dose was excreted in the urine as the parent drug during the first 24 hours following administration. In studies with healthy subjects and patients, the terminal half-life in plasma ranges between 3 and 5 hours. The ability of plerixafor to act as a substrate or as an inhibitor of P-glycoprotein has not been investigated.

Renal Impairment
Following a single 0.24 mg/kg SC dose, plerixafor clearance was reduced in subjects with varying degrees of renal impairment and was positively correlated with CL_{CR}. The mean $AUC_{0\text{-}24h}$ of plerixafor in subjects with mild (CL_{CR} 51-80 mL/min), moderate (CL_{CR} 31-50 mL/min), and severe (CL_{CR} < 31 mL/min) renal impairment was 7%, 32%, and 39% higher than healthy subjects with normal renal function, respectively. Renal impairment had no effect on C_{max}. A population pharmacokinetic analysis indicated an increased exposure ($AUC_{0\text{-}24h}$) in patients with moderate and severe renal impairment compared to patients with CL_{CR} > 50 mL/min. These results support a dose reduction of one-third in patients with moderate to severe renal impairment (CL_{CR} ≤ 50 mL/min) in order to match the exposure in patients with normal renal function. The population pharmacokinetic analysis showed that the mg/kg-based dosage results in an increased plerixafor exposure ($AUC_{0\text{-}24h}$) with increasing body weight; therefore if CL_{CR} is ≤ 50 mL/min the dose should not exceed 27 mg/day. *[see Dosage and Administration (2.3)]*

Since plerixafor is primarily eliminated by the kidneys, coadministration of plerixafor with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of plerixafor or the coadministered drug. The effects of coadministration of plerixafor with other drugs that are renally eliminated or are known to affect renal function have not been evaluated.

Race

Clinical data show similar plerixafor pharmacokinetics for Caucasians and African-Americans, and the effect of other racial/ethnic groups has not been studied.

Gender

Clinical data show no effect of gender on plerixafor pharmacokinetics.

Age

Clinical data show no effect of age on plerixafor pharmacokinetics.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies with plerixafor have not been conducted.

Plerixafor was not genotoxic in an *in vitro* bacterial mutation assay (Ames test in *Salmonella*), an *in vitro* chromosomal aberration test using V79 Chinese hamster cells, or an *in vivo* bone marrow micronucleus test in rats after subcutaneous doses up to 25 mg/kg (150 mg/m^2).

The effect of plerixafor on human fertility is unknown. The effect of plerixafor on male or female fertility was not studied in designated reproductive toxicology studies. The staging of spermatogenesis measured in a 28-day repeated dose toxicity study in rats revealed no abnormalities considered to be related to plerixafor. No histopathological evidence of toxicity to male or female reproductive organs was observed in 28-day repeated dose toxicity studies.

14 CLINICAL STUDIES

The efficacy and safety of Mozobil in conjunction with G-CSF in non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM) were evaluated in two placebo-controlled studies (Studies 1 and 2). Patients were randomized to receive either Mozobil 0.24 mg/kg or placebo on each evening prior to apheresis. Patients received daily morning doses of G-CSF 10 micrograms/kg for 4 days prior to the first dose of Mozobil or placebo and on each morning prior to apheresis. Two hundred and ninety-eight (298) NHL patients were included in the primary efficacy analyses for Study 1. The mean age was 55.1 years (range 29-75) and 57.5 years (range 22-75) in the Mozobil and placebo groups, respectively, and 93% of subjects were Caucasian. Three hundred and two (302) MM patients were included in the primary efficacy analyses for Study 2. The mean age

was 58.2 years (range 28-75) and 58.5 years (range 28-75) in the Mozobil and placebo groups, respectively, and 81% of subjects were Caucasian.

In Study 1, 59% of NHL patients who were mobilized with Mozobil and G-CSF collected $\geq 5 \times 10^6$ CD34+ cells/kg from the peripheral blood in four or fewer apheresis sessions, compared with 20% of patients who were mobilized with placebo and G-CSF ($p < 0.001$). Other CD34+ cell mobilization outcomes showed similar findings (Table 4).

Table 4: Study 1 Efficacy Results - CD34+ Cell Mobilization in NHL Patients

Efficacy Endpoint	Mozobil and G-CSF (n = 150)	Placebo and G-CSF (n = 148)	p-value[a]
Patients achieving $\geq 5 \times 10^6$ cells/kg in ≤ 4 apheresis days	89 (59%)	29 (20%)	< 0.001
Patients achieving $\geq 2 \times 10^6$ cells/kg in ≤ 4 apheresis days	130 (87%)	70 (47%)	< 0.001

[a]p-value calculated using Pearson's Chi-Squared test

The median number of days to reach $\geq 5 \times 10^6$ CD34+ cells/kg was 3 days for the Mozobil group and not evaluable for the placebo group. Table 5 presents the proportion of patients who achieved $\geq 5 \times 10^6$ CD34+ cells/kg by apheresis day.

Table 5: Study 1 Efficacy Results – Proportion of Patients Who Achieved $\geq 5 \times 10^6$ CD34+ cells/kg by Apheresis Day in NHL Patients

Days	Proportion[a] in Mozobil and G-CSF (n=147[b])	Proportion[a] in Placebo and G-CSF (n=142[b])
1	27.9%	4.2%
2	49.1%	14.2%
3	57.7%	21.6%
4	65.6%	24.2%

[a]Percents determined by Kaplan Meier method
[b]n includes all patients who received at least one day of apheresis

In Study 2, 72% of MM patients who were mobilized with Mozobil and G-CSF collected $\geq 6 \times 10^6$ CD34+ cells/kg from the peripheral blood in two or fewer apheresis sessions, compared with 34% of patients who were mobilized with placebo and G-CSF ($p < 0.001$). Other CD34+ cell mobilization outcomes showed similar findings (Table 6).

Table 6: Study 2 Efficacy Results – CD34+ Cell Mobilization in Multiple Myeloma Patients

Efficacy Endpoint	Mozobil and G-CSF (n = 148)	Placebo and G-CSF (n = 154)	p-value[a]
Patients achieving $\geq 6 \times 10^6$ cells/kg in ≤ 2 apheresis days	106 (72%)	53 (34%)	< 0.001
Patients achieving $\geq 6 \times 10^6$ cells/kg in ≤ 4 apheresis days	112 (76%)	79 (51%)	< 0.001
Patients achieving $\geq 2 \times 10^6$ cells/kg in ≤ 4 apheresis days	141 (95%)	136 (88%)	0.028

[a]p-value calculated using Pearson's Chi-Squared test

The median number of days to reach $\geq 6 \times 10^6$ CD34+ cells/kg was 1 day for the Mozobil group and 4 days for the placebo group. Table 7 presents the proportion of patients who achieved $\geq 6 \times 10^6$ CD34+ cells/kg by apheresis day.

Table 7: Study 2 – Proportion of Patients Who Achieved $\geq 6 \times 10^6$ CD34+ cells/kg by Apheresis Day in MM Patients

Days	Proportion[a] in Mozobil and G-CSF (n=144[b])	Proportion[a] in Placebo and G-CSF (n=150[b])
1	54.2%	17.3%
2	77.9%	35.3%
3	86.8%	48.9%
4	86.8%	55.9%

[a]Percents determined by Kaplan Meier method
[b]n includes all patients who received at least one day of apheresis

Multiple factors can influence time to engraftment and graft durability following stem cell transplantation. For transplanted patients in the Phase 3 studies, time to neutrophil and platelet engraftment and graft durability were similar across the treatment groups.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each single-use vial is filled to deliver 1.2 mL of 20 mg/mL solution containing 24 mg of plerixafor.

NDC Number: 58468-0140-1

- Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F). [see USP Controlled Room temperature]
- Each vial of Mozobil is intended for single use only. Any unused drug remaining after injection must be discarded.

17 PATIENT COUNSELING INFORMATION

Advise patients of the signs and symptoms of potential systemic reactions such as urticaria, periorbital swelling, dyspnea, or hypoxia during and following Mozobil injection. *[see Adverse Reactions (6.1)]*

Patients should inform a health care professional immediately if symptoms of vasovagal reactions such as orthostatic hypotension or syncope occur during or shortly after their Mozobil injection. *[see Adverse Reactions (6.1)]*

If patients experience itching, rash, or reaction at the site of injection, they should notify a health care professional as these symptoms have been treated with over-the-counter medications during clinical trials. *[see Adverse Reactions (6.1)]*

Inform patients that Mozobil may cause gastrointestinal disorders, including diarrhea, nausea, vomiting, flatulence, and abdominal pain. Patients should be told how to manage specific gastrointestinal disorders and to inform their health care professional if severe events occur following Mozobil injection. *[see Adverse Reactions (6.1)]*

Advise female patients with reproductive potential to use effective contraceptive methods during Mozobil use. *[see Warnings and Precautions (5.5) and Use In Specific Populations (8.1)]*

Manufactured by: Patheon UK Ltd., Swindon, UK

Manufactured for: Genzyme Corporation, 500 Kendall Street, Cambridge, MA 02142 USA

EXHIBIT C

In re patent of Gary J. Bridger et al.
USP 5,583,131
Approved Product: MOZOBIL™ (plerixafor)
Application for Patent Term Extension
Customer No. 22852

US005583131A

United States Patent [19]

Bridger et al.

[11] **Patent Number: 5,583,131**

[45] **Date of Patent: Dec. 10, 1996**

[54] **AROMATIC-LINKED POLYAMINE MACROCYCLIC COMPOUNDS WITH ANTI-HIV ACTIVITY**

[75] Inventors: **Gary J. Bridger**, West Chester; **Sreenivasan Padmanbhan**, Exton; **Renato T. Skerlj**, West Chester; **David M. Thornton**, Reading, all of Pa.

[73] Assignee: **Johnson Matthey Public Limited Company**, London, United Kingdom

[21] Appl. No.: **244,863**

[22] PCT Filed: **Dec. 16, 1992**

[86] PCT No.: **PCT/GB92/02334**

§ 371 Date: **Aug. 18, 1994**

§ 102(e) Date: **Aug. 18, 1994**

[87] PCT Pub. No.: **WO93/12096**

PCT Pub. Date: **Jun. 24, 1993**

[30] **Foreign Application Priority Data**

Dec. 16, 1991 [GB] United Kingdom 91/26677

[51] **Int. Cl.**[6] **C07D 401/14**; C07D 403/10; A61K 31/395; A61K 31/555

[52] **U.S. Cl.** **514/183**; 514/184; 540/465; 540/474

[58] **Field of Search** 540/465, 474; 514/183, 184

[56] **References Cited**

U.S. PATENT DOCUMENTS

5,021,409	6/1991	Murrer et al.	514/183
5,374,416	12/1994	Rousseaux	424/2

FOREIGN PATENT DOCUMENTS

92/16494 10/1992 WIPO .

OTHER PUBLICATIONS

Ciampolini et al, Inorganic Chem. 26(21), (1987), pp. 3527–3533.

Schneider et al, Helvitica Chimica Acta 69(1), (1986), pp. 53–61.

Yaouanc et al, J. Chem. Soc. Chem. Commun. (1991), pp. 206–207.

Primary Examiner—Philip I. Datlow

Attorney, Agent, or Firm—Cushman Darby & Cushman, L.L.P.

[57] **ABSTRACT**

Polyamine macrocyclic compounds, e.g. of 10 to 15 ring members and 3 to 6 ring amine nitrogens, linked through methylene groups to an aromatic moiety, show high selective activity against HIV.

35 Claims, No Drawings

AROMATIC-LINKED POLYAMINE MACROCYCLIC COMPOUNDS WITH ANTI-HIV ACTIVITY

This application is the 356USC371 Nation Stage of PCT/GB92/02334, filed Dec. 16, 1992.

This invention concerns improvements in chemical compounds, more especially it concerns compounds and pharmaceutical compositions. In particular it concerns compositions and compounds having activity in in vitro tests on Human Immunodeficiency Virus-infected cells.

The disease known as Acquired Immune Deficiency Syndrome (AIDS) caused by infection by HIV has attracted immense research effort because of the effects of the disease on infected individuals and the dangers of the disease spreading to a wider section of the population. In general, although various chemo-therapeutic treatments have been advocated, and some compounds have emerged as a potential basis for treatment, there is still a need for alternatives. In particular, most treatments such as the compound known as AZT have a high toxicity to cells, and it would be desirable to find compounds which are less toxic. In man, the development of resistance to AZT has been identified as an additional clinical problem.

We have found a group of compounds which show protective properties in vitro screens of cells challenged with HIV-1 and/or HIV-2, and are therefore useful for the treatment of AIDS and AIDS Related Complex and other vital and especially retrovital infections. Accordingly, the present invention provides the use of compounds defined below, in phamaceutical compositions for treating HIV-infected patients. The invention further provides pharmaceutical compositions comprising a said compound in combination or association with a pharmaceutically acceptable diluent or excipient, for the treatment of HIV-infected patents. The invention may also be defined as the use of a said compound for the manufacture of a medicament for the treatment of HIV-infected patients. The invention further provides a process for the production of a pharmaceutical composition for the treatment of a HIV-infected patient, comprising the combination of a compound as defined below with a pharmaceutically acceptable diluent or excipient, and formulating said composition into a form suitable far administration to said patient. The invention also provides a method of treatment of an HIV-infected patient, comprising administering to said patient an effective dose of a said compound. It is to be understood that treatment includes prophylactic treatment of patients at risk, in view of the protective properties observed. The use of the compounds may also be stated as a method of treating HIV-infected or HIV-challenged human cells to prevent or modulate the multiplication of the HIV, comprising administering to said cells an effective dose of a said compound. Whilst this description is especially directed to combating HIV, this invention includes other aspects in which other diseases may be treated, including for example microbial infections.

A 2,2'-dimer of cyclam has been reported as being isolated as a 2% by-product in the synthesis of cyclam (1,4,8,11-tetraaza-cyclotetradecane) (Barefield et al, J C S Chem Con (1981), 302). This compound was stated to be insoluble in water. We believe that the insoluble 2,2'-bicyclam is a mixture of the 2R,2'R and 2S,2'S enantiomers; we have characterised a soluble dimer which we believe to be the me, so 2R,2'S isomer. The 6,6'-bicyclam isomer has been reported by Fabbrizzi et al, Inorg Chem 25, 2671 (1986). Certain N,N'-linked bicyclic compounds have been reported by Ciampolini et al, Inorg Chem 26, 3527 (1987). No biological activity has been suggested for such compounds.

U.S. Pat. No. 4,156,683 discloses monocyclic and bicyclic macrocyclic compounds, which axe said to have biological activity in regulating sodium, potassium and calcium levels in mammals. Additionally, a specific group of N-alkylated monocyclic compounds are said to possess activity against A_2 influenza viruses in a modified Hermann test on chick fibroblast tissue. It is also said that the preferred compounds, which form complexes of greater stability, are those having three bridging chains between bridgehead nitrogen atoms, that is fused bicyclic compounds.

EP-A-0296522 discloses certain functionally modified cyclic polyamines, including that known as "cyclam", which complexes with rhodium and may be bound to an antibody or antibody fragment The aromatic-linked cyclic polyamines which form the subject of the present invention are not disclosed, nor is any anti-vital activity.

EP-A-0305320 also discloses several modified cyclic polyamines, but does not disclose identical cyclic polyamines linked together.

WO-A-9105762 discloses polyamines useful for their multi-point chelating activity, but does not disclose linked cyclic polyamines.

WO-A-9216494 is in the same name as the present applicants, and discloses long-chain polyamines, optionally linked to a cyclic polyamine, as agents active against HIV. No molecules having two cyclic polyamines, linked through an aromatic linker are disclosed in this prior art.

Our U.S. Pat. No. 5,021,409 (equivalent to EP-A-0434385) describes linked cyclic compounds as being active against HIV-1 and HIV-2 in in vitro tests. We have now discovered that certain of the linked cyclic compounds exhibit surprisingly improved activity against HIV. Thus, the present invention concerns a selected group of the compounds taught in said USP, having activity of at least an order of magnitude greater than the compounds tested in said USP.

The present invention provides as active compounds linked cyclic compounds of the general formula I

$$Z\text{-}R\text{-}A\text{-}R'\text{-}Y \qquad (I)$$

in which Z and Y are identical cyclic polyamine moieties having from 9 to 20 ring members and from 3 to 6 amine nitrogens in the ring spaced by 2 or more carbon atoms from each other,

A is an aromatic or heteroaromatic moiety other than quinoline, and

R and R' are each methylene linked to an amine nitrogen atom in Z and in Y, the amine nitrogens being otherwise unsubstituted. The invention also encompasses acid addition salts and metal complexes of the compounds of formula I.

In the above formula, the cyclic polyamine moieties may be substituted or unsubstituted, and suitable substituents are alkyl and/or aryl groups, eg of up to 10 carbon atoms, and any other atoms or groups which do not substantially adversely affect the activity or toxicity of the compounds. Preferred moieties are those of 10 to 15 ring members, and there are preferably 3 or 4 amine nitrogen atoms.

The aromatic or heteroaromatic moiety A tethers Y and Z through the linking groups R and R'. Moiety A may be phenyl or fused aromatic such as napthyl, heterocyclic such as pyridyl or thiophenyl, fused heterocyclic or joined aromatic and/or joined heteroaromatic, for example biphenyl or bipyridyl respectively. The moieties A may also be substituted at single or multiple non-linking positions with electron-donating groups, eg alkyl, thio, thioalkyl, hydroxyl,

alkoxyl, amino and derivatives thereof, or electron-withdrawing groups or atoms, eg nitro, halogen, carboxy, carboxamido, sulfonic acid and derivatives thereof.

The invention also includes what may be termed "pro-drugs", that is protected forms of the linked cyclic compounds, which release the compound after administration to a patient. For example, the compound may carry a protective group which is split off by hydrolysis in body fluids, eg in the bloodstream, thus releasing active compound. A discussion of pro-drugs may be found in "Smith and Williams' Introduction to the Principles of Drug Design", H. J. Smith, Wright, 2nd Edition, London 1988.

A few of the active compounds according to the invention axe known, (see Inorg Chem 26 (1987), p 3527–3533 and J Chem Soc, Chem Commun, (1991), 206, 207).

Accordingly, certain of the compounds of formula I are novel. The invention accordingly provides novel linked cyclic polyamine compounds of general formula Ia,

Z-R-A'-R'-Y (Ia)

in which Z, Y, R and R' are as defined above, with R and R' linked to nitrogen atoms in Z and Y, and

A' is an aromatic or heteroaromatic moiety which is unsubstituted or substituted, other than quinoline, provided that

A' is not unsubstituted phenylene when Z and Y are 14-membered tetraaza rings,

and their acid addition salts and metal complexes.

The invention further provides a method for the production of the compounds of formula Ia, which method comprises nucleophilic attack by cyclic polyamines Z' and Y' each having a single unprotected ring amine nitrogen, all other ring amine nitrogens being protected, on a compound of formula II

X-R-A'-R'-X II

wherein R, R' and A' are as defined above, and

each X is an active substituent which can be displaced by the unprotected amine nitrogens of polyamines Z' and Y' and is preferably selected from Br, Cl, I, methanesulfonate, 4-tolylsulfonate and trifluoromethane sulfonate,

and subsequently deprotecting the ring amine nitrogens.

It is well within the capabilities and knowledge of the skilled synthetic chemist to protect the amine nitrogens of cyclic polyamines, and it is preferred to use substitution by methanesulfonyl and/or 4-talylsulfonyl and/or diethylphosphoryl. The compounds of formula II are known.

The reaction is preferably carried out by reacting two equivalents of the protected polyamine with the compound of formula II in a solvent, such as acetonitrile or dimethylformamide, tetrahydrofuran or dioxane and in the presence of a base, for example sodium carbonate or potassium carbonate. The reaction generally takes place readily at room temperature to elevated temperature, to give a linked molecule having protected amine nitrogen atoms. In general, a mixture of products will be obtained, and we have found that chromatography on silica gel is a particularly convenient method of separation.

The deprotection step is suitably carried out by refluxing the protected molecule in a mixture of aqueous HBr and acetic acid or in the case of diethylphosphoryl in the presence of hydrogen chloride (gas) in THF or dioxane.

The compounds are indicated for the treatment of vital infections, especially retrovirus infections and particularly HIV infections, and the compounds of formula I are to he considered as active compounds for the pharmaceutical compositions, processes for making the same and methods of treatment mentioned above. In these aspects of the invention, it is to be understood that meso forms, enantiomers and resolved optically active forms of the compounds of formula I are included. Also, it is to he considered within the invention, compounds of formula I diluted with non-toxic or other active substances.

Acid addition salts, for example hydrochlorides, and non-toxic labile metal complexes of the compounds of formula I are also active compounds according to the present invention. Non-toxic in the present context has to be considered with reference to the prognosis for the infected patient without treatment. Copper and zinc complexes are preferred although other metals such as nickel may be considered, whereas less labile metal atoms such as cobalt and rhodium are less preferred because of likely lower selectivity.

The present invention will now be illustrated by the following preparative examples.

EXAMPLE 1

a) 2,3,5,6- Tetrafluoro-p-xylene-∝,∝'-diol

To a stirred solution of perfluoroterephthalic acid (1.0 g, 4.2 mmol) in anhydrous THF (10 ml) under an atmosphere of dry argon was added Borane. THF complex (1.0M solution in THF, 10 equivalents, 42 ml) dropwise, and the mixture stirred at room temperature overnight. The solution was evaporated under reduced pressure to give a colourless oil and the excess Borane destroyed by addition of anhydrous methanol (40 ml) and evaporation (repeated three times). The residue was treated with 5% aqueous hydrochloric acid then the pH of the mixture was adjusted to pH9 with 1N aqueous sodium hydroxide solution and extracted with dichloromethane (3×50 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to give 2,3,5,6-tetrafluoro-p-xylene-∝,∝'-diol (0.75 g, 86%) as a white solid. This was used without further purification.

b) 2,3,5,6- Tetrafluoro-p-xylene-∝,∝'-diol dimesylate

To a stirred solution of 2,3,5,6-tetrafluoro-p-xylene-∝,∝'-diol (0.72 g, 3.4 mmol) in dichloromethane (40 ml) containing triethylamine (1.2 ml, 2.5 equivalents) was added methanesulfonyl chloride (0.58 ml, 2.2 equivalents) dropwise at 0° C. and the mixture was allowed to warm to room temperature overnight. The solution was washed with saturated aqueous sodium bicarbonate solution (2×20 ml) and brine (2×20 ml) then dried ($MgSO_4$) and evaporated under reduced pressure. The residue was suspended in ether and filtered giving 2,3,5,6-tetrafluoro-p-xylene-∝,∝'-diol dimesylate (0.9 g, 72%) as a white solid.

c) 1,1'-[2,3,5,6-Tetrafluoro-1,4-phenylenebis-(methylene)]-bis-tris(p-toluenesulfonyl)-1,4,8,11-tetraazacyclotetradecane

2,3,5,6-Tetrafluoro-p-xylene-∝,∝'-diol dimesylate (150 mg, 0.4 mmol), tris-(p-toluenesulfonyl)-1,4,8,11-tetraazacyclotetradecane monohydrate 826 mg, 1.2 mmol, 3.0 equivalents) and potassium carbonate (252 mg, 3.0 equivalents) in anhydrous acetonitrile (20 ml) were heated to reflux with stirring under argon for 48 hours until all the dimesylate starting material had been consumed; confirmed by TLC (silica gel, 2% methanol in dichloromethane as eluent). The mixture was evaporated under reduced pressure and the residue was dissolved in ethyl acetate (40 ml) and washed with saturated aqueous sodium bicarbonate solution (2×20 ml) and brine (2×20 ml) then dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography

on silica gel during with 2% methanol in dichloromethane giving a white foam identified by ^{1}H NMR and FAB-MS as 1,1'-[2,3,5,6-tetrafluoro-1,4-phenylene-bis-(methylene)]-bis-tris-(p-toluenesulfonyl)-1,4,8,11-tetraazacyclotetradecane $C_{70}H_{86}N_8O_{12}S_6F_4$ requires C, 56.05; H, 5.78; N, 7.47; found C, 55.81; H, 5.73; N, 7.36.

d) 1,1'-[2,3,5,6-Tetrafluoro-1,4-phenylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane

1,1'-[2,3,5,6-Tetrafluoro-1,4-phenylenebis-(methylene)]-bis-tris-(p-toluenesulfonyl)-1,4,8,11-tetraazacyclotetradecane (200 mg, 0.13 mmol) was dissolved in a mixture of acetic acid and hydrobromic acid (48%) in a ratio of approximately 3:2 by volume (10 ml) and heated to 100° C. for 24 hours during which time a white solid precipitated. The mixture was allowed to cool and the solid was filtered off and washed with acetic acid and ether and dried in vacuo giving a white solid identified by ^{1}H NMR, FAB-MS and elemental analysis as 1,1'-[2,-3,5,6-tetra-fluoro-1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclo-tetradecane octahydrobromide dihydrate (65 mg, 40%).

$C_{28}H_{62}N_8O_2Br_8F_4$ requires C, 26.73; H, 4.96; N, 8.90; found C, 26.84; H, 5.05; N, 8.21.

The following compounds were prepared using analogous methods to those described above in steps b)-d):

5-Nitro-m-xylene-α,α'-diol gave 1,1-[5-Nitro-1,3-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane octahydrobromide dihydrate. $C_{28}H_{65}N_9O_4Br_8$ requires C, 27.31; H, 5.31; N, 10.24; found C, 27.49;, H, 5.26; N, 9.75.

2,4,5,6-Tetrachloro-m-xylene-α,α'-diol gave 1,1'-[2,4,5,6-tetrachloro-1,3-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraaza-cyclotetradecane octahyclrobromide dihydrate.

$C_{28}H_{62}O_2Cl_4Br_8$, requires C, 25.40; H, 4.71; N, 8.46; found C, 25.72; H, 4.76; N, 8.05.

EXAMPLE 2

a) α,α'-Dibromo-1,4-dimethylnaphthalene

To a solution of 1,4-dimethylnaphthalene (0.5 g, 3.2 mmol) and benzoyl peroxide (0.08 equivalents, 62 mg) in carbon tetrachloride (20 ml) was added N-bromosuccinimide (1.14 g, 2.0 equivalents) and the mixture was heated to reflux for 24 hours during which time a white solid precipitated. The mixture was faltered hot (to remove the succinimide by-product) and then allowed to cool over several hours during which time a white cystalline solid precipitated. The solid was filtered off and dried giving 1,4-dimethylnaphthalene-α,α'-dibromide (473 mg, 50%).

The following compound was prepared using methods analogous to steps c) and d) of Example 1:

1,4-Dimethylnaphthalene-4,4'-dibromide gave 1,1'-[1,4-naphthylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane octahydrobromide tetrahydrate.

$C_{32}H_{72}N_8O_4Br_8$ requires C, 30.20; H, 5.69;, N, 8.81; found C, 30.28; H, 5.52; N, 8.66.

EXAMPLE 3

a) 1-Benzyl-5,13-di-(p-toluenesulfonyl)-9-methanesulfonyl-1,5,9,13-tetraazacyclohexadecane.

To a solution of N,N-bis-[3-(p-toluenesulfonylamidopropyl)-]benzylamine hydrochloride (25 g) (NL Patent 6603655) in dry DMF (800 ml) under argon was added sodium hydride (10 equivalents) in small portions over 3 hours. When the addition was complete the solution was heated at 6° C. for 1 hour then allowed to cool and the excess sodium hydride was removed by filtration under argon. The filtrate was transferred to another dry flask and the solution was then heated to 100°–110° C. and bis-propanolamine-trimethanesulfonate [P Moore, J Chem Soc Dalton Trans 1985 (7) 1361–1364] (1.0 equivalent) in DMF (500 ml) was added dropwise over 8 hours with rapid stirring. The temperature was maintained at 100°–110° C. for a further 16 hours, allowed to cool then the mixture was poured into iced water (1500 ml) and the resulting off-white precipitate that formed was collected by filtration. The solid was dissolved in dichloromethane (250 ml) and the solution was washed with water (5×50 ml), then dried ($MgSO_4$) and evaporated under reduced pressure to give a yellow oil. Trituration with ethanol (200 ml) gave a white crystalline solid which was filtered off, washed with a small volume of ethanol, then ether and dried in vacuo to give 1-benzyl-5,-13-di-(p-toluenesulphonyl)-9-methanesulphonyl- 1,5,9,-13tetraazacyclohexadecane (45%), identified by ^{1}H NMR and FAB-MS.

b) 1,9-Di-(p-toluenesulfonyl)-5-methanesulfonyl-1,5,9,13-tetraazacyclohexadecane

To a solution of 1-benzyl-5,13-di-(p-toluene-sulfonyl)-9-methanesulfonyl-1,5,9,13-tetraazacyclohexadecane in formic acid (20 ml) was added Palladium hydroxide on carbon (Pearlmans catalyst, 4.0 g) and the resulting suspension was heated to reflux for 72 hours with stirring. The mixture was allowed to cool, then filtered through celite and the filtrate was evaporated under reduced pressure. The colourless oil which remained was dissolved in dichloromethane (50 ml) and washed with 10% aqueous sodium hydroxide solution (2×20 ml), and water (2×20 ml) then dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with 3% methanol in dichloromethane giving a white solid identified by ^{1}H NMR and FAB-MS as 1,9-di-(p-toluenesulphonyl-5-methanesulfonyl-1,5,9,13-tetraaza-cyclohexadecane.

The mono-deprotected tetraazacyclohexadecane macrocycle described in step b) was used as described in Example 1 steps c) and d), to prepare tetraazacyclohexadecane dimers.

The following compounds were prepared in this manner.

4,4'-Dibromo-m-xylene gave 1,1'-[1,3-phenylene-bis-(methylene)]-bis-1,5,9,13-tetraazacyclohexadecane octahydrobromide hexahydrate.

$C_{32}H_{72}N_8O_6Br_8$ requires C, 29.2; H, 6.15; N; 8.54; found C, 29.37; H, 5.50; N, 7.90.

4,4'-Dibromo-p-xylene gave 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,5,9,13-tetraazacyclohexadecane octahydrobromide hexahydrate.

$C_{32}H_{76}N_8O_6Br_8$ requires C, 29.29; H, 6.15; N, 8.54; found. C, 28.96; H, 5,47; N,7.96.

Other compounds which may be made according to the invention are:

1,1'-[1,3-phenylenebis(methylene)]-bis-1,5,9,13-tetraazacyclohexadecane

1,1'-[1,3-phenylenebis(methylene)]-bis-1,5,9-triazacyclododecane

1,1'-[1,4-phenylenebis(methylene)]-bis-1,5,9-triazacyclododecane

EXAMPLE 4

Synthesis of Compound F

1,1'-[1,4-Phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane zinc dichloride monohydrate

To a stirred solution of 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane (1 g) in methanol (25 ml) was added zinc(II) chloride (0.54 g, 2.0 eq) in

methanol (5 ml). Towards the end of the addition a white precipitate formed. Sufficient methanol and water were added to give a homogenous solution and the mixture was then evaporated in vacuo. The solid residue was suspended in a mixture of methanol/ether and filtered giving 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane zinc dichloride monohydrate (1.45 g, 94%) as a white powder.

$C_{28}H_{56}Cl_4OZn_2$ requires; C, 42.38; H, 7.11; N, 14.12; Cl, 17.88: found; C, 42.64; H, 7.14; N, 14.18; Cl, 17.89.

EXAMPLE 5

Synthesis of Compound G

1,1'-[1,4-Phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane copper diacetate hexahydrate

To a stirred solution of 1,1'[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane (100 mg) was added copper(II) acetate (72 mg, 2.0 eq) in one portion. The solution became dark blue/purple in colour almost immediately. The mixture was stirred for one hour then triturated with ether to give a blue precipitate. The blue solid was filtered off and dried giving 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane copper diacetate hexahydrate (80 mg, 46%).

$C_{36}H_{80}N_8O_{Cu2}$ requires; C, 43.58; H, 8.13; N, 11.29; found: C, 43.24; H, 7.88; N, 11.13.

EXAMPLE 6

1,1'-[3'-Biphenylene-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,8,11tetraazacyclotetradecane

A mixture of 3,3'-bis-(bromomethyl)-1,1'-biphenyl [W. Wenner, *J. Org. Chem.* (1952), 17, 525–528], (200 mg, 0.59 mmol), anhydrous potassium carbonate (325 mg, 2.35 mmol, 4 eq) and tris-(p-toluene-sulphonyl)-1,4,8,11-tetraazacyclotetradecane (801 mg, 1.18 mmol, 2 eq) in anhydrous acetonitrile (15 ml) was stirred at 50° C. under argon. After 6 hours the reaction mixture was allowed to cool; dichloromethane (75 ml) was added and the resulting solution filtered. The filtrate was evaporated in vacuo to yield a glassy white solid. Chromatography of the crude product on a column of silica gel (2.5 cm×20 cm), eluting with methanol/dichloromethane 1:160 v/v gave a white solid, identified by ^{1}H NMR as 1,1'-[3,3'-biphenylene-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (665 mg, 76%).

Synthesis of Compound J

1,1'-[3,3'-Biphenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane octahydrobromide tetrahydrate

The per-tosylated derivative from above (450 mg, 0.30 mmol) was dissolved in glacial acetic acid (9 ml). Hydrobromic acid (~48% w/v, Aldrich, 3.5 ml) was added and the resulting mixture heated to reflux. After 24 hours the dark brown solution was cooled in an ice bath over 2 hours during which time an off-white precipitate formed. The precipitate was collected by centrifugation and washed with glacial acetic acid (3×10 ml) followed by diethyl ether (4×10 ml) then dried overnight in vacuo to give a white powder, identified by ^{1}H NMR and elemental analysis as 1,1'-[3,3'-biphenylene-bis-(methylene)]-bis-1,4,8,11-tetraaza-cyclotetradecane octahydrobromide tetrahydrate (194 mg, 50%). $C_{34}H_{74}N_8Br_8O_4$ requires; C, 31.46; H, 5.70; N, 8.63; found; C, 31.30; H, 5.68; N, 8.60.

EXAMPLE 7

1,1'-[4,4'-(2,2'-Bipyridine)-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacydotetradecane

A mixture of 4,4'-bis-(bromomethyl)-2,2'-bipyridine [T J Meyer, Inorg. Clam. (1991), 30, 2942–2949], (200 mg, 0.57 mol), anhydrous potassium carbonate (314 mg, 2.27 mmol, 4 eq) and tris-(p-toluenesulfonyl)-1,4,8,11-tetraazacyclotetradecane (774 mg, 1.14 mmol, 2 eq) in anhydrous acetonitrile (20 ml) was stirred at 50° C. under argon for 2 hours. The mixture was allowed to cool and dichloromethane (100 ml) was added and the resulting solution filtered through celite. The filtrate was evaporated in vacuo to give a yellow glassy solid which was purified by column chromatography on silica gel (3×20 cm column) using triethylamine/methanol/dichloromethane 1:1:100 v/v as eluent. A glassy white solid was obtained, identified by ^{1}H NMR as 1,1'-[4,4'-(2,2'-bipyridine)-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (600 mg, 70%).

Synthesis of Compound K

1,1'-[4,4'-(2,2'-Bipyridine)-bis-(methyl)]-bis-1,4,8,11-tetraazacyclotetradecane decahydrobromide pentahydrate

The per-tosylate derivative from above (570 mg, 0.38 mmol) was dissolved in glacial acetic acid (6.5 ml). Hydrobromic acid (~48% w/v, Aldrich, 3.0 mmol) was added and the mixture heated to reflux for 24 hours. The resulting dark brown solution was cooled in an ice bath over 2 hours) during which time an off-white precipitate formed. The precipitate was collected by centrifugation and washed with glacial acetic acid (3×10 ml) followed by diethyl ether (5×10 ml) and dried overnight in vacuo to give a white powder identified by ^{1}H NMR and elemental analysis as 1,1'-[4,4'-(2,2'-bipyridine)-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane decahydrobromide pentahydrate (450 mg, 81%).

$C_{32}H_{76}N_{10}Br_{10}O_5$ requires; C, 25.97; H, 5.17; N, 9.46; found; C, 26.07; H, 4.57; N, 9.47.

EXAMPLE 8

1,1'-[2,9-(1,10-Phenanthroline)-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane

A mixture of 2,9-bis-(bromomethyl)-1,10-phenanthroline [C J Chandler, J. Heterocycl. Chem. (1981), 18, 599–601], (200 mg, 0.54 mmol), anhydrous potassium carbonate (300 mg, 2.17 mmol, 4 eq) and axis-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (740 mg, 1.09 mmol, 2 eq) in anhydrous acetonitrile (20 ml) were stirred at 50° C. under argon for 3 hours. The mixture was allowed to cool and dichloromethane (100 ml) was added and the resulting solution filtered through celite. The filtrate was evaporated in vacuo to give a yellow glassy solid which was purified by column chromatography on silica gel (3×2 cm column) using triethylamine/methanol/dichloromethane 1:3:100 v/v eluent. A pale yellow solid was obtained, identified by ^{1}H NMP as 1,1'-[2,9-(1,10-phenamhroline)-bis-(methylene)]-

bis-tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (575 mg, 69%).

Synthesis of Compound L

1,1'-[2,9-(1,10-Phenanthroline)-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane decahydrobromide trihydrate

The per-tosylated derivative from above (400 mg, 0.26 mmol) was dissolved in glacial acetic acid (8 ml). Hydrobromic acid (48% w/v, Aldrich, 3.5 ml) was added and the mixture was heated to reflux for 16 hours. The resulting dark brown solution was cooled in an ice bath over 2 hours during which time an off-white precipitate formed. The precipitate was collected by centrifugation then purified by re-precipitation from a mixture of hydrobromic acid (~48% w/v, 2 ml) and water (2 ml) with glacial acetic acid (5 ml). The white solid was again collected by centrifugation, washed with glacial acetic acid (3×10 ml) and diethyl ether (4×10 ml) and finally dried overnight in vacuo to give a white powder, identified by ^{1}H NMR and elemental analysis as 1,1'-[2,9-(1,10-phenanthroline)-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane decahydrobromide trihydrate (80 mg, 21%).

$C_{34}H_{72}N_{10}Br_{10}O_3$ requires; C, 27.82; H, 4.94; N, 9.54; found; C, 27.81; H, 4.97; N, 9.17.

EXAMPLE 9

This compound and corresponding intermediates axe described by T. A. Kaden, Helv. Chim. Acta., (1985), 69, 53–61. An alternative procedure is given below.

11,11'-[1,4-Phenylene-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,7,11-tetraazacyclotetradecane

A mixture of α,α'-dibromo-p-xylene (249 mg, 0.94 mmol), anhydrous potassium carbonate (652 mg, 4.71 mmol, 5 eq) and tris(p-toluenesulphonyl)-1,4,7,11-tetraazacyclotetradecane [T. A. Kaden, Heir. Chim. Acta., (1983), 66, 861–870] (1.25 g, 1.89 mmol, 2 eq) in anhydrous acetonitrile (15 ml) was heated at 50° C. with stirring under argon for 18 hours. The reaction mixture was allowed to cool and dichloromethane (50 ml) was added and the resulting solution filtered through celite. The filtrate was evaporated in vacuo to give a white foam which was purified by column chromatography on silica gel using methanol/dichloromethane (1:40 v/v) as eluent. A white solid was obtained, identified by ^{1}H NMR as 11,11'-[1,4-phenylene-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,7,11-tetraazacyclotetradecane (1.0 g, 74%)

Synthesis of Compound M

11,11'-[1,4-Phenylene-bis-(methylene)]-bis-1,4,7,11-tetraazacyclotetradecane octahydrobromide dihydrate

The per-tosylated derivative from above (500 mg, 0.35 mmol) was dissolved in glacial acetic acid (7 ml). Hydrobromic acid (~48% w/v, 4 ml) was added and the resulting mixture heated to reflux for 20 hours. Further glacial are fie acid (10 ml) was added and the solution was cooled in an ice bath over 1 hour during which time a white precipitate formed. The solid was collected by centrifugation and washed with glacial acetic acid (2×10 ml) followed by diethyl ether (4×10 ml) and dried overnight in vacuo to give a white powder, identified by ^{1}H NMR and elemental analysis as 11,11'-[1,4-phenylene-bis-(methylene)]-bis-1,4,7,11-tetraazacyclotetradecane octahydrobromide dihydrate (280 mg, 67%).

$C_{28}H_{66}N_8Br_8O_2$ requires; C, 28.35; H, 5.61; N, 9.45; found; C, 28.34; H, 5.42; N, 9.02.

EXAMPLE 10

11[(1, Methylene-4-bromomethylene)-phenylene]-tris-(p-toluenesulphonyl)-1,4,7,11-tetraazacyclotetradecane

A mixture of α,α'-dibromo-p-xylene (3.98 g, 15.1 mmol, 10 eq), and anhydrous potassium carbonate (417 mg, 3.02 mmol, 2 eq) in anhydrous acetonitrile (20 ml) was heated to 50° C. With rapid stirring a solution of tris-(p-toluenesulphonyl)-1,4,7,11-tetraazacyclotetradecane (1.0 g, 1.51 mmol) in anhydrous acetonitrile (20 ml) was added dropwise over 4 hours. After a further 1 hour the reaction mixture was allowed to cool and the solvent evaporated in vacuo. The residue was purified by column chromatography on silica gel (5×20 cm), eluting with a gradient of dichloromethane to methanol/dichloromethane 1:20 v/v over 2 liters total elution volume. To the resulting colourless glass was added dry hexane (150 ml) and the mixture was heated to reflux then allowed to cool to room temperature. The precipitate which formed was filtered, washed with hexane (3×10 ml) followed by diethyl ether (20 ml) and dried overnight in vacuo to give the title compound as a white powder (710 mg, 53%).

1,11'-[1,4-Phenylene-bis-(methylene)]-tris-(p-tohenesulphonyl)-1,4,8,11-tetraazacyclotetradecane)-tris-(p-toluenesulphonyl)-1,4,7,11-tetraazacyclotetradecane

A mixture of 11-[(1-methylene-4-bromomethylene)-phenylene]-tris-(p-tohenesulphonyl)-1,4,7,11-tetraacyclotetradecane (350 mg, 0.41 mmol), anhydrous potassium carbonate (230 mg, 1.66 mmol, 4 eq) and tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (422 mg, 0.62 mmol, 1.5 eq) in anhydrous acetonitrile (20 ml) were heated with stirring at 50° C. under argon for 7 hours. The reaction mixture was allowed to cool and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (2.5×25 cm column) using methanol/dichloromethane (1:60 v/v) as eluent, followed by preparative thin layer chromatography on silica gel (eluent methanol/dichloromethane 1:40 v/v, 20 mg/plate) to give a colourless glass, identified by ^{1}H NMR as the title compound (130 mg, 30%).

Synthesis of Compound N

1,11'-[1,4-Phenylene-bis-(methylene)]-1,4,8,11-tetraazacyclotetradecane-1,4,7,11-tetraazacydotetradecane octahydrobromide hexahydrate

The per-tosylated derivative from above (115 mg, 0.08 mmol) was dissolved in glacial acetic acid (3 ml). Hydrobromic acid (~48%, Aldrich, 1.5 mmol) was added and the mixture was heated to reflux for 48 hour. The resulting dark brown solution was cooled in an ice bath and a white precipitate formed. The solid was collected by centrifugation and washed with glacial acetic acid (3×10 ml) followed by diethyl ether (5×10 ml) and dried overnight in vacuo to give a white powder, identified by ^{1}H NMR and elemental analysis as 1,11'-[1,4-phenylene-bis-(methylene)]-1,4,8,11-

tetraazacyclotetradecane-1,4,7,11-tetraaza-cyclotetradecane octahydrobromide hexahydrate. (71 mg, 75%). $C_{29}H_{74}N_8Br_8O_6$ requires; C, 26.73; H, 5.93; N, 8.91; found; C, 26.50; H. 5.69; N, 9.31.

EXAMPLE 11

1,1'-[2,6-Pyridinebis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane

A stirred solution of 2,6-bis(bromomethyl)pyridine hydrobromide [M. E. Haeg, B. J. Whitlock and H. W. Whitlock Jr, J. Ant. Chem. Soc., (1989), 111, 692], (131 mg, 0.378 mmol), tris-(p-toluene-sulphonyl)-1,4,8,11-tetraazacyclotetradecane (500 mg, 0.75 mmol) and potassium carbonate (400 mg, 2.88 mmol) in anhydrous acetonitrile (15 ml) was heated at 80° C. for 22 hours under an atmosphere of arson. The reaction mixture was allowed to cool to room temperature and concentrated in vacuo. The residue was purified by column chromatography on silica gel using 3% methanol in dichloromethane as eluent thus affording a pale white solid which was identified by ^{1}H NMP, and FAB-MS as 1,1'-[2,6-pyridinebis-(methylene)]-bis-tris(p-toluene-sulphonyl)-1,4,8,11-tetraacyclotetradecane (500 ml, 93%).

Mass spectrum (FAB); m/e (relative intensity); 1428 (M+1, 100), 1272 (35)

Synthesis of Compound O

1,1'-[2,6-Pyridinebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane octahydrobromide tetrahydrate

To a stirred solution of 1,1'-[2,6-pyridinebis-(methylene)]-bis-tris(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (500 mg, 0.35 mmol) in acetic acid (16 ml) was added 48% hydrobromic add (12 ml) and the solution heated to 110° C. for 48 hours during which time a white solid precipitated. The reaction mixture was allowed to cool to mom temperature and the solid was filtered off, washed with acetic acid followed by ether and dried in vacuo thus affording a white solid which was identified by ^{1}H NMR, ^{13}C NMR, FAB-MS and elemental analysis as 1,1'-[2,6-pyridinebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane octahydrobromide tetrahydrate (230 mg, 65%).

$C_{27}H_{69}N_9O_4Br_8$ requires; C, 26.50; H, 5.64; N, 10.31; Br, 52.29; found C, 26.91; H, 5.31; N, 10.08; Br, 51.99. Mass spectrum (FAB); m/e (relative intensity); 586 (M+HBr, 48), 584 (M+HBr, 50), 504 (M+1, 100), 201 (60).

EXAMPLE 12

1,1'-[3,5-Pyridine-bis-(methylene)]-bis-tris(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane

A stirred solution of 3.5-bis(bromomethyl)pyridine hydrobromide (M. Momenteau, J. Mispelter, B. Loock and J. M. Lhoste, J. Chem. Soc. Perkin Trans. 1, (1985), 61], (131 mg, 0.37 mmol) , tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (500 mg, 0.755 mmol) and potassium carbonate (400 mg, 2.88 mmol) in anhydrous dimethylformamide (15 ml) were heated at 70° C. for 21 hours under an atmosphere of argon. The reaction mixture was allowed to cool to room temperature and concentrated in vacuo. The residue was purified by column chromatography on silica gel using 2% methanol in dichloromethane as eluent thus affording a white foamy solid which was identified by ^{1}H NMR and FAB-MS as 1,1'-[3,5-pyridinebis-(methylene)]-bis-tris(p-toluenesulphonyl)-1,4,8,11-tetraaza-cyclotetradecane (320 mg, 78%).

Mass spectrum (FAB); m/e (relative intensity); 1428 (M+1, 100), 1272 (45).

Synthesis of Compound P

1,1'[3,5-Pyridinebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane nonahydrobromide dihydrate

To a stirred solution of 1,1'-[3,5-pyridinebis-(methylene)-bis-tris(p-tohenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (320 mg, 0.224 mmol) in acetic acid (12 ml) was added 48% hydrobromic acid (8 ml) and the solution heated to 100° C. for 48 hours during which time a white solid precipitated. The reaction mixture was allowed to cool to room temperature and the solid was filtered off, washed with acetic add followed by ether and dried in vacuo thus affording a white solid which was identified by ^{1}H NMR, ^{13}C NMR, FAB-MS and elemental analysis as 1,1 '-[3,5-pyridinebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane nonahydrobramide dihydrate (150 mg, 53%).

$C_{27}H_{66}N_9O_2Br_9$ requires; C, 25.56; H, 5.21; N, 9.94; Br, 56.74; found C, 25.71; H, 5.25; N, 9.76; Br, 56.28. Mass spectrum (FAB); m/e (relative intensity); 586 (M+HBr, 39), 584 (M+HBr, 41), 504 (M+1, 60), 201 (100).

EXAMPLE 13

1,1'-[1,3-Phenylenebis-(methylene)]-bis-tris(p-toluenesulphonyl)-1,4,7,10-tetraazacyclododecane

A stirred solution of α,α'-dibromo-m-xylene (125 mg, 0.472 mmol), tris-(p-tohenesulphonyl)-1,4,7,10-tetraazacyclododecane [M. F. Tweedle et al, Inorg. Chem., (1992), 30, 1265], (600 mg, 0,945 mmol) and potassium carbonate (400 mg, 2.88 mmol) in anhydrous acetonitrile (15 ml) were heated to reflux for 6 hours under an atmosphere of argon. The resulting cloudy white solution was allowed to cool to room temperature and the solids collected by filtration and washed with acetonitrile. The solid residue was dissolved in a mixture of dichloromethane (100 ml) and water (15 ml). The organic phase was separated and washed with water (15 ml), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was dried in vacuo thus affording a white foamy solid which was identified by ^{1}H NMR as 1,1'-[1,3-phenylenebis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,7,10-tetraazacyclododecane (330 mg, 51%).

Synthesis of Compound Q

1,1'-[1,3-Phenylenebis-(methylene)]-bis-1,4,7,10-tetraazacyclododecane hexahydrobromide

To a stirred solution of 1,1'-[1 ,3-phenylenebis-(methylene)]-bis-tris-(p-toluenesulfonyl)-1,4,7,10-tetraazacyclododecane (330 mg, 0.24 mmol) in anhydrous methanol/tetrahydrofuran (1:2, 15 ml) was added 3% sodium amalgam (20 g) and dibasic sodium phosphate (400 mg). The reaction mixture was vigorously stirred under argon at 70° C. for 41 hours. The reaction mixture was allowed to cool to room temperature and the supernatent solution was separated from the solids by decantation then concentrated in vacuo. Chloroform (50 ml) and water (5 ml) were added to the residue and the aqueous phase was extracted with chloroform (3×50 ml). Concentration of the combined organic fractions afforded quantitatively a viscous oil which was identified by

1H NMR as 1,1'-[1,3-phenylenebis-(methylene)]-bis-1,4,7,10-tetraazacyclododecane.

Into a stirred solution of 1,1'-[1,3-phenylenebis-(methylene)]-bis-1,4,7,10-tetraazacyclododecane in ethanol (20 ml, 95%) was bubbled HBr gas for 15 minutes resulting in an immediate white precipitate. The white solid was filtered off, washed with ethanol and ether and immediately dried in vacuo for 48 hours thus affording a white solid which was identified by ^{1}H NMR, ^{13}C NMR, FAB-MS and elemental analysis as 1,1'-[1,3-phenylene-(methylene)]-bis-1,4,7,10-tetraazacyclo-dodecane hexahydrobromide (130 mg, 63%).

$C_{27}H_{52}N_8Br_6$ requires C, 30.92; H, 5.62; N, 12.02; Br, 51.43; found C, 31.09; H, 5.80; N, 11.90; Br, 51.17. Mass spectrum (FAB); m/e (relative intensity); 529 (M+HBr, 53), 527 (M+HBr, 55), 447 (M+I, 100), 277 (40), 185 (35).

EXAMPLE 14

1,1'-[1,4-Phenylenebis-(methylene)]-bis-tris(p-toluenesulphonyl)-1,4,7,10-tetraazacyclododecane

A stirred solution of α,α'-dibromo-p-xylene (99 mg, 0.374 mmol), tris-(p-toluenesulphonyl)-1,4,7,10-tetraazacyclododecane (475 mg, 0.748 mmol) and potassium carbonate (320 mg, 2.24 mmol) in anhydrous acetonitrile (15 ml) was heated at reflux for 1.4 hours under an atmosphere of argon. The resulting cloudy white solution was allowed to cool to room temperature and the solids collected by filtration and washed with acetonitrile. The solid residue was dissolved in a mixture of dichloromethane (120 ml) and water (15 ml). The organic phase was separated and washed with water (15 ml), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was dried in vacuo thus affording a white solid which was identified by ^{1}H NMR as 1,1'-[1,4-phenylenebis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,7,10-tetraazacyclododecane (360 mg, 70%).

Mass spectrum (FAB); m/e (relative intensity); 1371 (IVI+1, 12), 1217 (8).

Synthesis of Compound R

1,1'-[1,4-Phenylenebis-(methylene)]-bis-1,4,7,10-tetraazacyclododecane hexahydrobromide

To a stirred solution of 1,1'-[1,4-phenylenebis-(methylene)-bis-tris(p-toluensulphonyl)-1,4,7,10-tetraazacyclododecane (360 mg, 0.262 mmol) in anhydrous methanol/dimethylsulphoxide (1:5, 18 ml) was added 3% sodium amalgam (23 g) and dibasic sodium phosphate (400 mg). The reaction mixture was vigorously stirred under argon at 100° C. for 4 hours then allowed to cool to room temperature and the supernatent solution was separated from the solids by decantation and concentrated in vacuo. Chloroform (50 ml) and water (5 ml) were added to the residue and the aqueous phase was extracted with chloroform (3×50 ml). Concentration of the combined organic fractions afforded quantitatively a foamy white solid which was identified by ^{1}H NMR as 1,1'-[1,4-phenylenebis-(methylene)]-bis-1,4,7,10-tetraazacyclododecane.

Into a stirred solution of 1,1'-[1,4-phenylenebis-(methylene)]-bis-1,4,7,10-tetraazacyclododecane in ethanol (15 ml, 95%) was bubbled HBr gas for 15 minutes resulting in an immediate white precipitate. The white solid was filtered off, washed with ethanol and ether and immediate dried in vacuo for 48 hours thus affording a white solid which was identified by ^{1}H NMR, ^{13}C NMR, FAB-MS and elemental analysis as 1,1'-[1,4-phenylenebis-(methylene)]-bis-1,4,7,10-tetra-azacyclododecane hexahydrobromide (115 mg, 44%).

$C_{27}H_{52}N_8Br_6$ requires C, 30.92; H, 5.62; N, 12.02; Br 51.43, found C, 30.90; H, 5.83; N, 11.83; Br, 51.19. Mass spectrum (FAB); m/e (relative intensity); 529 (M+HBr, 40), 527 (M+HBr, 40), 447 (M+1, 58), 185 (100).

EXAMPLE 15

1,1'-[2,5-Thiophene-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane

To a solution of tris-p-toluenesulphonyl-1,4,8,11-tetraazacyclotetradecane monohydrate (1.0 g, 1.5 mmol) and potassium carbonate (300 mg, 2.2 mmol) in acetonitrile (20 ml) was added 2,5-dichloromethyl thiophene [J. M. Griffing, L. F. Salisbury, J. Am. Chem. Soc., (1948), 70, 3416–3419], (137 mg, 0.76 mmol) and the mixture was heated to reflux overnight with rapid stirring. The mixture was allowed to cool and the solid was filtered off. The filtrate was evaporated in vacuo and the residue partitioned between methylene chloride (50 ml) and water (25 ml). The organic layer was separated, dried (Na_2SO_4) and evaporated in vacuo to give the crude product as a light brown solid. Column chromatography [silica gel; methylene chloride/methanol(40/1)] was used to isolate a white solid identified by ^{1}H NMR and FAB-MS as 1,1'-[2,5-thiophene-bis-(methylene)]-bis-tris-(p-tolueno-sulphonyl)-1,4,8,11-tetraazacyclotetradecane (315 mg, 29%).

Mass spectrum (FAB); M/e (relative intensity); 1434 (M+1, 49), 1277 (31). 772 (100), 616 (30), 508 (24).

Synthesis of Compound T

1,1'-[2,5-Thophenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane octahydrobromide

To a solution of 1.1'-[2,5-thiophene-bis-(methylene)]-bis-tris-(p-toluenesulphonyl)-1,4,8,11-tetraazacyclotetradecane (177 mg, 0.12 mmol) in acetic acid (6 ml) was added hydrobromic acid (Aldrich 48% aqueous, 4 ml) and the mixture was heated to a reflux with stirring for 16 hours during which time a light brown solid precipitated from a dark brown solution. On cooling, a further portion of acetic acid was added (10 ml) and the solids were filtered off, washed with acetic acid (10 ml) and ether (20 ml) and dried in vacuo giving a white solid identified by ^{1}H NMR and FAB-MS as 1,1'-[2,5-thiophene-bis-(methylene)-bis-1,4,8,11-tetraaza-cyclotetradecane octahyarobromide (82 mg, 97%),

Mass spectrum (FAB); m/e (relative intensity); 591 (M+HBr, 26), 589 (M+HBr, 26), 509 (M+1, 22) 311 (23), 201 (71), 185 (100).

The compounds of the invention were tested in a screen by the MTT method (I Vixol Methods 120: 309–321 [1988]). MT-4 cells (2.5×10^4/well) were challenged with HIV-1 (HTLV-IIIB) or HIV-2 (LAV-2 ROD) at a concentration of 100 $CCID_{50}$ and incubated in the presence of various concentrations of the test compounds, which were added immediately after challenge with the virus. After 5 days culture at 37° C. in a CO_2 incubator, the number of viable cells was assessed by the MTT (tetrazolium) method. Antiviral activity and cytotoxicity of the compounds are expressed in the table below as IC_{50} (μg/ml) and CC_{50} (μg/ml), respectively. The potential therapeutic usefulness was assessed by calculating a Selectivity Index (SI) corre-

sponding to the ratio of CC_{50} to IC_{50}. A control test was performed using the known anti-HIV treatment AZT.

In Table 1 below, the compounds screened were:

AZT: known anti-HIV compound

A: 1,1'-[1,3-phenylenebis(methylene)]bis-1,4,8,11-tetraazacyclotetradecane

B: 1,1'-[1,4-phenylenebis(methylene)]bis-1,4,8,11-tetraazacyclotetradecane

C: 1,1'-[5-nitro-1,3-phenylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane

D: 1,1'-[2,3,5,6-tetrafluoro-1,3-phenylene-bis-(methylene)]bis-1,4,8,11-tetraazacyclotetradecane

E: 1,1'-[1,4-naphthylenebis(methylene)]bis-1,4,8,11-tetraazacyclotetradecane

F–V: See preceding preparative Examples.

W: 1,1'-[2,5-dimethyl-1,4-phenylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane

X: 1,1'-[2,5-dichloro-1,4-phenylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane

Y: 1,1'-[2-bromo-1,4-phenylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane

Z: 1,1'-[6-phenyl-2,4-pyridinebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane

TABLE 1

	HIV-1 (III_B)			HIV-2 (ROD)		
CMPD	IC_{50} µg/ml	CC_{50} µg/ml	SI	IC_{50} µg/ml	CC_{50} µg/ml	SI
AZT Comparison	<0.008	>1	>125	—	—	—
A	0.03	>500	$>1.6 \times 10^4$	<0.01	>500	$>5 \times 10^4$
B	0.006	>500	$>8.3 \times 10^4$	<0.01	>500	$>5 \times 10^4$
C	0.05	55	1100	0.07	55	756
D	0.01	60	6000	0.01	60	6000
E	0.07	71	1014	0.05	71	1420
F	0.0026	>200	$>7.6 \times 10^4$	0.0019	>200	$>1 \times 10^5$
G	0.018	>200	$>1.1 \times 10^4$	0.027	>200	$>7.4 \times 10^3$
J	0.16	>200	>1250	0.22	>200	>900
K	0.38	117	300	0.35	117	334
L	0.29	>200	>690	0.32	>200	>625
M	0.03	>500	$>1.6 \times 10^4$	0.07	>500	$>7.1 \times 10^3$
N	0.01	>500	$>5 \times 10^4$	0.07	>500	$>7.1 \times 10^3$
O	0.03	>500	$>1.6 \times 10^4$	0.08	>500	$>6.2 \times 10^3$
P	0.04	>500	$>1.2 \times 10^4$	0.09	>500	$>5.5 \times 10^3$
Q	0.07	19	271	0.5	19	38
R	0.3	51	170	2.2	51	23
T	0.01	>500	$>5.0 \times 10^4$	0.02	>500	$>2.5 \times 10^4$
W	0.0076	>250	$>3.2 \times 10^4$	0.0013	>250	$>1.9 \times 10^5$
X	0.0131	71.87	5461	0.0030	72.66	2.4×10^4
Y	0.0075	>250	$>3.2 \times 10^4$	0.0043	>250	$>5.7 \times 10^4$
Z	0.0489	>250	5112	0.0246	>250	1.0×10^4

It can readily be seen that the compounds according to the invention are highly active against HIV-1 and -2, with low toxicity, in the in vitro tests used.

The compound B, which is the most preferred compound of the invention, was further tested for antiviral effects on different laboratory strains of HIV-1 in MT-4 cells, using the MIT assay. Compound B was found to have an IC_{50} in the range of 2–5 ng/ml against IIIb, RF, HE and NDK strains, showing that its high activity is remarkably strain-independent.

T4-lymphocytes and monocytes are targets for HIV-1 infection in vivo. The following test method showed that compound B inhibits virus replication also in primary T4 cells and primary monocytes in culture.

Primary T4 lymphocytes were purified from human spleens obtained from healthy donors by using a commercial kit ("Lympho-Kwik") which combines reaction of cells with specific monoclonal antibodies and density gradient centrifugation to separate the cells. Preparations obtained by this procedure contained 60–80% CD4 positive cells as analysed by FACS. Cells were stimulated with 2 µg/ml PHA for 24 hours. Then they were spun down and infected with HIV-1, strain IIIb, by suspending the cells 10-fold concentrated in virus solution. Adsorption was allowed for 2 hours at 37° C. The inoculum was removed by centrifugation and the cells were re-suspended at their original concentration in fresh culture medium containing IL-2 (40 IE/ml). Test compound was added after stimulation and virus adsorption. Every 3 to 4 days post infection half of the supernatant of the infected cultures was removed and replaced by fresh medium containing the test compound at the particular concentration, The concentration of vital p24 antigen was determined in the supernatent by means of a commercial ELISA kit (Coulter) and served as a parameter for virus production. Compound B does not interfere with the p24 Elisa test (highest concentration tested: 100 µg/ml).

Mononuclear cells were isolated from healthy, HIV-negative donors using Ficoll density separation. Cells (4×10^5/ml) were incubated for 5 days in 48 well plates (Costar) in monocyte medium consisting of RPMII640, supplemented with 20% ECS and 10% human serum. On day 5 non-adherent cells were washed out four times with warm PBS containing 2% human serum. Preparations obtained by the procedure were >95% positive for non-specific esterase (Sigma) and cell viability (as determined by trypan blue exclusion) was always >95%.

The monocytotropic strain of HIV-1, BaL, was used for the infection of these monocyte preparations (Pemo et al, 1 Exp Meal, 169, 933, 1989).

Adherent monocytes were exposed to 50 µg/well of a 1:30 dilution of HIV-1, BaL for 30 minutes subsequently, monocyte medium was added to 1 ml/well. Adsorption was allowed for 24 hours at 37° C. Then, the wells were washed twice in order to remove excess virus and were cultivated in the presence of different drug concentrations. Thus, test compounds were added after adsorption. Every 3 to 4 days post infection the supernatant of the infected cultures was removed and replaced by fresh medium containing the test compound at the particular concentration. The concentration of viral p24 antigen was determined as described above.

IC_{50} and IC_{90} values were calculated by comparing the p24 antigen concentrations in supernatent of treated, infected cells and uncreated, infected cells at days 11 and 14 post infection.

Table 2 shows that Compound B is a potent inhibitor of HIV-1 replication in both primary cell types, with IC_{90} values of 1–2 ng/ml. At the highest concentration tested, 100 ng/ml, no cytotoxicity was observed.

TABLE 2

Activity of Compound B and AZT against HIV-1, IIIb, replication in primary T4 lymphocytes and against HIV-1, BaL, replication in primary monocytes

Compound	Cell Type	IC_{50} (μg/ml) day 11	IC_{50} (μg/ml) day 14	IC_{90} (μg/ml) day 11	IC_{90} (μg/ml) day 14
B	Lymphocytes	<0.001	<0.001	<0.001	0.0010
AZT	Lymphocytes	0.00045	0.00043	0.0022	0.0011
B	Monocytes	<0.001	0.0011	0.0019	0.0021
AZT	Monocytes	0.0010	0.0010	0.0015	0.0017

Using the same methods, it was also shown that Compound B was a strong inhibitor of vital replication in primary T4 cells infected with low-passage primary clinical isolates of HIV-1 from three different geographical locations (K31, Zaire, D370, California, and K6/2, Germany).

The low cytotoxicity of Compound B was also shown by incubation of exponentially growing cells with Compound B or with AZT and determining cell numbers 2, 3 and 4 days after seeding. Compound B did not inhibit growth of MT4, MOLT4, HUT78, Jurkat cells (all T cell lines) nor the growth of the monocylic U937 cell line at concentrations below 300 μg/ml. With the exception of the HUT78 cells, AZT was in all cases more cytotoxic than Compound B with TC_{50} values (μg/ml) of 23, 37, 184 and 5 for MT4, MOLT4, Jurkat and U937 respectively.

In contrast to HIV-protease inhibitors, the compounds of the invention do not block virus production from chronically infected cells, indicating that the antiviral target is in the early part of the infection process, before, or at, integration of the provirus. To pinpoint the stage at which the compounds interact with the HIV replicative cycle, a time-of-addition experiment was carried out on MT4 cells infected with HIV-1 strain IIIb at high virus multiplicity to ensure that the virus replicative steps would be synchronised in the whole cell populations. Test compounds wife added 1, 2, 3, . . . 22, 23, 24 hours after infection, and vital p24 antigen production determined 29 hours after infection.

Depending on the stage at which compounds interact and the need for intracellular metabolism, addition of the compounds could be delayed for n hours without loss of activity. Daxtran sulphate, which acts at the virus adsorption step, must be added together with the virus (n=0) to be active. For AZT, which, following its intercellular phosphorylation, acts at the reverse transcriptase step, addition to the cells could be delayed until ca 4 hours (n=4) after infection. For the TIBO derivative (R82913), which does not need intracellular transformation before it can interact with reverse transcriptase the addition could be delayed by another 2 hours (n=6). The protease inhibitor Ro31-8959 which interacts with a late event in the virus cycle (assembly of mature virus) was still effective if added as late as 12 hours after infection (n=12). From the time-of-addition experiment appeared that for Compound B, n=1 or 2, so that the compound must interact with a process following virus absorption but preceding reverse transcription, for example, virus-cell fusion and/or uncoating.

To obtain further evidence for the inhibitory effect of Compound B on HIV uncoating (or fusion), experiments were designed whereby the viral RNA harvested from cells that had just been infected was monitored for its sensitivity to degradation by RNase. It was reasoned that if tincoating (fusion) was hampered, the viral capsid (or envelope) proteins would remain associated with the viral RNA genome and thus the RNA should be protected against RNase attack. When MT4 cells were exposed to radiolabelled viral particles at a very high multiple of infection and then treated with different concentrations of Compound B, viral RNA harvested from the cells 4 hours after infection showed resistance to degradation by RNaseA. Vital RNA harvested from HIV-infected cells treated with other anti-HIV agents (ie AZT, DDI, R82913, or Ro31–8959) did not show this increased resistance to degradation by RNase.

In addition, Compound B was also found to inhibit fusion, which is the mechanism by which viruses cnter cells and by which virus or infectious material is transmitted from cell to cell. Syncytium formation between chronically infected cells and uninfected cells reflects the gp120/41 mediated fusion process of vital entry. The syncytium inhibition assay (Baba et al, J AIDS 3 493, 1990)) using HIV-1 IIIb infected HUT78 cells with MOLT4 cells indicates that Compound B is at least as potent as dextran sulphate in inhibition of fusion. The concentrations required (approximately 1 μg/ml) are considerably higher than the antiviral IC_{50} values, but are well below cytotoxicity levels.

These results strongly indicate that the compounds of the invention inhibit primarily the uncoating step and also to some extent the fusion step of the vital replicative cycle. This is a unique mode of action for anti-HIV agents, and the involvement of two distinct target steps makes it less likely that resistance to the drug will develop rapidly in treated patients.

Although no suitable animal models exist for the testing of in vivo efficacy of anti-HIV agents, testing of drug serum levels in the rabbit was carried out, and after sc administration of 10 mg/kg of Compound B, samples of rabbit serum were taken. Measurement of anti-HIV activity in the sen showed levels of the drug exceeding the in vitro IC_{50} level by a factor of a hundred for at least 6 hours after administration. This indicates that the compound would have anti-HIV activity in humans or an animal susceptible to infection by HIV.

The compounds of Formula I axe therefore useful for the treatment and/or prophylaxis of HIV infection, alone or in combination with other active agents. The appropriate dosage will, of course, vary depending upon, for example, the compound of Formula I employed, the host, the mode of administration and the nature and severity of the conditions being treated. However, in general, satisfactory results in humans are indicated to be obtained at daily dosages from about 0.01–20 mg/kg of body weight. An indicated daily dosage in humans is in the range from about 0.7 mg to about 1400 mg of a compound of Formula I conveniently administered for example in divided doses up to four times a day.

The compounds of Formula I may be administered by any conventional route, particularly enterally, preferably orally, eg in the loan of tablets or capsules or in liquid form, eg as a syrup; or parenterally, eg in the form of solutions or suspensions for iv or sc administration.

Compound B is the preferred compound of Formula I. In view of its activity in the test methods as described above, it is indicated that Compound B may be administered to humans at daily dosages of from 2 to 200 mg, preferably 10 to 70 mg, by parentexal administration, eg by subcutaneous injection.

The compounds of Formula I may be administered in free base form or in pharmaceutically acceptable acid addition salt or metal complex form. Such salts and complexes may be prepaxed in conventional manner as described in the Examples, and exhibit the same order of activity as the free bases. Pharmaceutical compositions containing compounds of Formula I may be manufactured in conventional manner. Unit dosage forms contain for example from about 0.5 mg

to about 100 mg of a compound of Formula I in free base or pharmaceutically acceptable acid addition salt form.

We claim:

1. A pharmaceutical composition active against HIV comprising as an active ingredient a linked cyclic compound of formula I,

Z-R-A-R'-Y (I)

in which Z and Y are identical cyclic polyamine moieties having from 10 to 15 ring members and from 3 to 6 amine nitrogens in the ring spaced by 2 or more carbon atoms from each other, said amine nitrogens being the only ring heteroatoms,

A is an aromatic or heteroaromatic moiety other than quinoline,

R and R' are each methylene linked to nitrogen atoms in Z and Y,

the amine nitrogen atoms being otherwise unsubstituted.

2. A composition according to claim 1, wherein in the compound of formula I, each moiety Z and Y has 14 ring members and 4 amine nitrogens in the ring.

3. A composition according to claim 1, wherein the active ingredient is 1,1'-[1,3-phenylenebis(methylene)]-bis-1,4,8,11-tetra-azacyclotetradecane in acid addition salt form.

4. A composition according to claim 1, wherein the active ingredient is 1,1'-[1,4-phenylenebis(methylene)]-bis-1,4,8,11-tetra-azacyclotetradecane in acid addition salt form.

5. A composition according to claim 1, wherein the active ingredient is a bis-zinc complex of 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane.

6. A composition according to claim 1, wherein the active ingredient is a bis-copper complex of 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane.

7. A composition according to claim 1, wherein the active ingredient is 1,1'-[3,3'-biphenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

8. A composition according to claim 1, wherein the active ingredient is 11,11'-[1,4-phenylene-bis-(methylene)]-bis-1,4,7,1 1-tetraazacyclotetradecane in acid addition salt form.

9. A composition according to claim 1, wherein the active ingredient is 1,11'-[1,4-phenylene-bis-(methylene)]-1,4,8,11-tetraazacyclotetradecane-1,4,7,11-tetraazacyclotetradecane in acid addition salt form.

10. A composition according to claim 1, wherein the active ingredient is 1,1'-[2,6-pyridine-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

11. A composition according to claim 1, wherein the active ingredient is 1,1-[3,5-pyridine-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

12. A composition according to claim 1, wherein the active ingredient is 1,1'-[2,5-thiophene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

13. A composition according to claim 1, wherein the active ingredient is 1,1'-[4,4'-(2,2'-bipyridine)-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

14. A composition according to claim 1, wherein the active ingredient is 1,1'-[2,9-(1,10-phenanthroline)-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

15. A composition according to claim 1, wherein the active ingredient is 1,1'-[1,3-phenylene-bis-(methylene)]-bis-1,4,7,10-tetraazacyclotetradecane in acid addition salt form.

16. A composition according to claim 1, wherein the active ingredient is 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,7,10-tetraazacyclotetradecane in acid addition salt form.

17. The compound of claim 1, which is 1,1'-[5-nitro-1,3-phenylenebis(methylene)]bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

18. The compound of claim 1, which is 1'1'-[2,4,5,6-tetrachloro-1,3-phenyleneis(methylene)]bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

19. The compound of claim 1, which is 1,1'-[2,3,5,6-tetrafluoro-1,4-phenylenebis(methylene)]bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

20. The compound of claim 1, which is 1,1'-[1,4-naphthylene-bis-(methylene)]bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

21. The compound of claim 1, which is 1,1'-[1,3-phenylenebis-(methylene)]bis-1,5,9-triazacyclododecane in acid addition salt form.

22. The compound of claim 1, which is 1,1'-[1,4-phenylene-bis-(methylene)]-1,5,9-trlazacyclododecane in acid addition salt form.

23. The compound of claim 1, which is a bis-zinc complex of 1,1'[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane.

24. The compound of claim 1, which is 1,1'-[3,3'-biphenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

25. The compound of claim 1, which is 1,1'-[2,6-pyridine-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

26. The compound of claim 1, which is 1,1'-[3,5-pyridine-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

27. The compound of claim 1, which is 1,1'-[2,5-thiophene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

28. The compound of claim 1, which is 1,1'-[4,4'-(2,2'-bipyridine)-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

29. The compound of claim 1, which is 1,1'-[2,9-(1,10-phenanthroline)-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane in acid addition salt form.

30. The compound of claim 1, which is 1,1'-[1,3-phenylene-bis-(methylene)]-bis-1,4,7,10-tetraazacyclotetradecane in acid addition salt form.

31. The compound of claim 1, which is 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,7,10-tetraazacyclotetradecane in acid addition salt form.

32. The compound of claim 1, which is 1,1'-[2,5-dimethyl-1,4-phenylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane.

33. The compound of claim 1, which is 1,1'-[2,5-dichloro-1,4-phenylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane.

34. The compound of claim 1, which is 1,1'-[2-bromo-1,4-phenylenebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane.

35. The compound of claim 1, which is 1,1'-[6-phenyl-2,4-pyridinebis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane.

* * * * *

EXHIBIT D

In re patent of Gary J. Bridger et al.
USP 5,583,131
Approved Product: MOZOBIL™ (plerixafor)
Application for Patent Term Extension
Customer No. 22852

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Customer No 204 | ISTMT | DATE PRINTED 01/22/2009

COMPUTER PACKAGES, INC.
414 HUNGERFORD DRIVE
ROCKVILLE MD 20850

MAINTENANCE FEE STATEMENT

According to the records of the U.S.Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O.Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
5,583,131	**$1,955.00**	**$0.00**	**06/10/08**	**08/244,863**	**12/10/96**	**08/18/94**	**12**	**YES**	**204835MBUS11**

Return To:

USPTO Home Page

Finance Online Shopping Page

United States Patent and Trademark Office

Patent Bibliographic Data

02/03/2009 01:19 PM

Patent Number:	5583131		**Application Number:**	08244863	
Issue Date:	12/10/1996		**Filing Date:**	08/18/1994	
Title:	AROMATIC-LINKED POLYAMINE MACROCYCLIC COMPOUNDS WITH ANTI-HIV ACTIVITY				
Status:	4th, 8th and 12th year fees paid			**Entity:**	Large
Window Opens:	N/A	**Surcharge Date:**	N/A	**Expiration:**	N/A
Fee Amt Due:	Window not open	**Surchg Amt Due:**	Window not open	**Total Amt Due:**	Window not open
Fee Code:					
Surcharge Fee Code:					

Most recent events (up to 7):

01/26/2009	Payor Number Assigned.
01/26/2009	Payer Number De-assigned.
01/23/2009	Pat Hldr no Longer Claims Small Ent Stat
01/22/2009	Payment of Maintenance Fee under 1.28(c).
06/16/2008	Maintenance Fee Reminder Mailed.
06/10/2008	Payment of Maintenance Fee, 12th Yr, Small Entity.
06/10/2004	Payment of Maintenance Fee, 8th Yr, Small Entity.
	--- End of Maintenance History ---

Address for fee purposes:

GENZYME CORPORATION
LEGAL DEPARTMENT
15 PLEASANT ST CONNECTOR
FRAMINGHAM, MA
017019322

Run Another Query

Need Help? | USPTO Home Page | Finance Online Shopping Page

EXHIBIT E

In re patent of Gary J. Bridger et al.
USP 5,583,131
Approved Product: MOZOBIL™ (plerixafor)
Application for Patent Term Extension
Customer No. 22852

Entry No.	Document Date	Product(s)	Country	Document Type	Document Title	Application Type(s)
1	04 May 1998	Mozobil	United States	Application	Mozobil IND 55,851 original submission: AMD3100	IND
2	08 May 1998	Mozobil	United States	Serial	Serial 0001, General Correspondence:Contact Information Sent to FDA Regarding Mozobil IND 55,851	IND
3	04 Aug 1998	Mozobil	United States	Serial	Serial 0002 to IND 55,851, Protocol Amendment, Revised Phase I Protocol 98-01 for Mozobil.	IND
4	29 Aug 1998	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
5	08 Oct 1998	Mozobil	United States	Serial	Serial 0003, Protocol Amendment, Change in Protocol 98-01 for Mozobil IND 55,851.	IND
6	08 Oct 1998	Mozobil	United States	Serial	Serial 0004 Response to FDA Request for Information Regarding Mozobil IND 55,851, Clinical Development Plan of Phase I Protocol 98-01	IND
7	08 Oct 1998	Mozobil	United States	Serial	Serial 0005, Information Amendment Pharm-Tox - Final Reports from Pre-clinical Study for Mozobil IND 55,851.	IND
8	29 Jan 1999	Mozobil	United States	Serial	Serial 0006, Protocol Amendment Change in Protocol 98-01 for Mozobil IND 55,851.	IND
9	29 Jan 1999	Mozobil	United States	Serial	Serial 0007, Protocol Amendment New Protocol - Protocol 2001 for Mozobil IND 55,851.	IND
10	01 Mar 1999	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
11	24 Mar 1999	Mozobil	United States	Serial	Serial 0008, Information Amendment Clinical - Amendment 4 to Protocol 98-01 for Mozobil IND 55,851.	IND
12	21 Apr 1999	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
13	21 Apr 1999	Mozobil	United States	Correspondence Received	Correspondence Received Regarding Mozobil IND 55,851 Protocol AMD3100-2001	IND
14	01 Jul 1999	Mozobil	United States	Serial	Serial 0010 for Mozobil IND 55,851, Protocol Amendment New Investigator and Response to FDA Request for Information Regarding Protocol AMD3100-2001.	IND
15	05 Jul 1999	Mozobil	United States	Serial	Serial 0009 ANNUAL REPORT for Mozobil IND 55,851 for Reporting Period May 1998 through May 1999.	IND
16	16 Aug 1999	Mozobil	United States	Serial	Serial 0011 Protocol Amendment for Mozobil IND 55,851, Change in Protocol - Amendment 1 to AMD3100- 2001.	IND
17	20 Aug 1999	Mozobil	United States	Correspondence Received	Correspondence Received FDA Salvage Therapy in Clinical Trials	IND
18	23 Aug 1999	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
19	15 Sep 1999	Mozobil	United States	Serial	Serial 0012 to Mozobil IND 55,851 Safety Report - Protocol AMD3100-2001 Report Number AMD3100-01001 Patient	IND
20	24 Sep 1999	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55,851 for Mozobil.	IND
21	07 Oct 1999	Mozobil	United States	Serial	Serial 0013 to Mozobil IND 55,851 Safety Report - Protocol AMD3100-2001 Report Number AMD3100-01001 Patient	IND
22	15 Mar 2000	Mozobil	United States	Serial	Serial 0014 to Mozobil IND 55,851 Safety Report - Protocol AMD3100-2001 Report Number AMD3100-02001 Patient	IND
23	15 Mar 2000	Mozobil	United States	Serial	Serial 0015 to Mozobil IND 55,851 Safety Report - Protocol AMD3100-2001 Report Number AMD3100-02002 Patient	IND

24	15 Mar 2000	Mozobil	United States	Serial	Serial 0016 to Mozobil IND 55,851 Safety Report - Protocol AMD3100-2001 Patient Follow-up to Serial	IND
25	17 Apr 2000	Mozobil	United States	Serial	Serial 0017, Protocol Amendment to Mozobil IND 55,851, Change in Protocol Amendment 2 to AMD3100-2001.	IND
26	08 May 2000	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
27	31 May 2000	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
28	05 Jul 2000	Mozobil	United States	Serial	Serial 0018 IND 55,851 Mozobil Annual Report, to Cover the Reporting Period From 5 May 1999 to 5 May 2000.	IND
29	25 Jul 2000	Mozobil	United States	Serial	Serial 0019 for Mozobil IND 55,851, Response to FDA Request for Information. Summary Results From Cohort 1 and 2 From Study AMD3100-2001.	IND
30	11 Aug 2000	Mozobil	United States	Serial	Serial 0020 for Mozobil IND 55,851, Pharm/Tox Information Amendment. Summary of Nonclinical Studies and Reports.	IND
31	16 Aug 2000	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. RESPONSE TO SERIAL #19 CLINICAL COMMENTS FOR COHORT 1 AND 2 REPORTS FOR PROTOCOL AMD3100-2001 FROM	IND
32	16 Oct 2000	Mozobil	United States	Serial	Serial 0021 for Mozobil IND 55,851 - Protocol Amendment - New Protocol AMD3100-1002	IND
33	21 Nov 2000	Mozobil	United States	Serial	Serial 0022 to Mozobil IND 55,851 - Safety Report - Initial to Protocol 2001	IND
34	18 Dec 2000	Mozobil	United States	Serial	Serial 0023 to Mozobil IND 55,851 - Response to FDA Request for Information	IND
35	20 Dec 2000	Mozobil	United States	Serial	Serial 0024 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 3 to Protocol 2001	IND
36	22 Feb 2001	Mozobil	United States	Serial	Serial 0025 of Mozobil IND 55,851 - Protocol Amendment - New Investigator CV and FDA Form 1572	IND
37	22 Feb 2001	Mozobil	United States	Serial	Serial 0026 of Mozobil IND 55,851 - Protocol Amendment - New Investigator	IND
38	23 Feb 2001	Mozobil	United States	Serial	Serial 0027 of Mozobil IND 55,851 - Protocol Amendment - New Protocol AMD3100-2002	IND
39	23 Feb 2001	Mozobil	United States	Serial	Serial 0037 of Mozobil IND 55,851 - Annual Report - To Cover Reporting Period From 2000-05-05 Through 2001-05-05	IND
40	12 Mar 2001	Mozobil	United States	Serial	Serial 0028 of Mozobil IND 55,851 - Information Amendment Chemistry Microbiology - Amendment to Section 7-3 Drug Product	IND
41	16 Apr 2001	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND

42	16 Apr 2001	Mozobil	United States	Serial	Serial 0029 of Mozobil IND 55,851 - Response to FDA Request for Information - Summary of Pharmacokinetic Findings From Protocol 2001	IND
43	25 Apr 2001	Mozobil	United States	Serial	Serial 0030 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2001 Patient	IND
44	09 May 2001	Mozobil	United States	Serial	Serial 0031 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 2 to Protocol 1002	IND
45	10 May 2001	Mozobil	United States	Serial	Serial 0032 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2001 Patient	IND
46	25 May 2001	Mozobil	United States	Serial	Serial 0033 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 1 to Protocol 1002	IND
47	07 Jun 2001	Mozobil	United States	Serial	Serial 0034 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2001 Patient	IND
48	11 Jun 2001	Mozobil	United States	Serial	Serial 0035 of Mozobil IND 55,851 - Response to FDA Request for Information	IND
49	28 Jun 2001	Mozobil	United States	Serial	Serial 0036 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2001 Patient	IND
50	26 Jul 2001	Mozobil	United States	Serial	Serial 0038 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 2 to Protocol 1002	IND
51	24 Aug 2001	Mozobil	United States	Serial	Serial 0039 of Mozobil IND 55,851 - Response to FDA Request for Information	IND
52	24 Sep 2001	Mozobil	United States	Serial	Serial 0040 of Mozobil IND 55,851 - Protocol Amendment - New Protocol AMD3100-1003	IND
53	11 Oct 2001	Mozobil	United States	Serial	Serial 0041 for Mozobil IND 55,851 - General Correspondence	IND
54	16 Oct 2001	Mozobil	United States	Serial	Serial 0042 to Mozobil IND 55,851 - Protocol Amendment Change in Protocol - Amendment Number 1 to Protocol 1003	IND
55	16 Oct 2001	Mozobil	United States	Serial	Serial 0043 to Mozobil IND 55,851 - Other - Revisions to FDA Forms 1572	IND
56	01 Nov 2001	Mozobil	United States	Serial	Serial 0044 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2001	IND
57	14 Nov 2001	Mozobil	United States	Serial	Serial 0045 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 3 to Protocol 1002	IND
58	18 Dec 2001	Mozobil	United States	Serial	Serial 0046 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 4 to Protocol 1002	IND
59	03 Jan 2002	Mozobil	United States	Serial	Serial 0047 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 2 to Protocol 1003	IND
60	25 Jan 2002	Mozobil	United States	Serial	Serial 0048 of Mozobil IND 55,851 - Other - Revisions to FDA Forms 1572	IND

61	04 Feb 2002	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
62	06 Feb 2002	Mozobil	United States	Serial	Serial 0049 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 3 to Protocol 1003	IND
63	11 Feb 2002	Mozobil	United States	Serial	Serial 0050 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2001 Patient	IND
64	20 Feb 2002	Mozobil	United States	Serial	Serial 0051 of Mozobil IND 55,851 - Other - Revisions to FDA Forms 1572	IND
65	22 Feb 2002	Mozobil	United States	Serial	Serial 0052 of Mozobil IND 55,851 - Protocol Amendment - New Protocol AMD3100-1004	IND
66	25 Feb 2002	Mozobil	United States	Serial	Serial 0053 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 4 to Protocol 1003	IND
67	26 Feb 2002	Mozobil	United States	Serial	Serial 0054 of Mozobil IND 55,851 - Other - Form FDA 1572 and CV for	IND
68	27 Feb 2002	Mozobil	United States	Serial	Serial 0055 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Correction of Amendment Number 4 to Protocol 1003	IND
69	08 Mar 2002	Mozobil	United States	Serial	Serial 0056 of Mozobil IND 55,851 - Protocol Amendment - New Protocol AMD3100-1005	IND
70	21 Mar 2002	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55,851 for Mozobil.	IND
71	22 Mar 2002	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
72	22 Mar 2002	Mozobil	United States	Serial	Serial 0057 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 5 to Protocol 1003	IND
73	22 Mar 2002	Mozobil	United States	Serial	Serial 0058 of Mozobil IND 55,851 - Other - Changes to Forms FDA 1572 for Protocol 1002	IND
74	26 Mar 2002	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
75	03 Apr 2002	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55,851 for Mozobil.	IND
76	04 Apr 2002	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
77	15 Apr 2002	Mozobil	United States	Serial	Serial 0059 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 1 to Protocol 1005	IND
78	17 Apr 2002	Mozobil	United States	Serial	Serial 0060 of Mozobil IND 55,851 - Information Amendment Clinical - Summary of Safety Data From Clinical Studies and Preliminary Data for Protocols 1002 and 1003	IND
79	22 Apr 2002	Mozobil	United States	Serial	Serial 0061 for Mozobil IND 55,851 - Safety Report - Initial Nonclinical	IND
80	23 Apr 2002	Mozobil	United States	Serial	Serial 0062 to Mozobil IND 55,851 - Protocol Amendment Change in Protocol - Amendment Number 1 to Protocol 1004	IND
81	09 May 2002	Mozobil	United States	Serial	Serial 0063 to Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 6 to Protocol 1003	IND

82	15 May 2002	Mozobil	United States	Serial	Serial 0064 of Mozobil IND 55,851 - Protocol Amendment and Other - Change in Protocol Amendment Number 2 to Protocol 1004 - Version 5.0 of Investigator's Brochure	IND
83	16 May 2002	Mozobil	United States	Serial	Serial 0065 of Mozobil IND 55,851 - Information Amendment - Pharmacology Toxicology Draft Reports and Summaries with Appendices, Including In Vitro, Cardiovascular, Dose Range Finding and Toxicology Studies	IND
84	10 Jun 2002	Mozobil	United States	Serial	Serial 0066 of Mozobil IND 55,851 - Annual Report - To Cover Reporting Period From 2001-05-06 Through 2002-05-01	IND
85	11 Jun 2002	Mozobil	United States	Serial	Serial 0067 of Mozobil IND 55,851 - General Correspondence - Decision to Terminate Study 2001	IND
86	18 Jun 2002	Mozobil	United States	Serial	Serial 0068 of Mozobil IND 55,851 - Potocol Amendment - Change in Protocol Amendment 2 to Protocol AMD3100-1005	IND
87	27 Jun 2002	Mozobil	United States	Serial	Serial 0069 of Mozobil IND 55,851 - Protocol Amendment New Protocol - AMD3100-2101	IND
88	19 Jul 2002	Mozobil	United States	Serial	Serial 0070 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amenedment Number 7 to Protocol 1003	IND
89	19 Jul 2002	Mozobil	United States	Serial	Serial 0071 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 3 to Protocol 1005	IND
90	29 Jul 2002	Mozobil	United States	Serial	Serial 0072 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 8 to 1003	IND
91	29 Jul 2002	Mozobil	United States	Serial	Serial 0073 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 4 to Protocol 1005	IND
92	07 Aug 2002	Mozobil	United States	Serial	Serial 0074 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Nimber 3 to Protocol 1004	IND
93	08 Aug 2002	Mozobil	United States	Serial	Serial 0075 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 4 to Protocol 1004	IND
94	09 Aug 2002	Mozobil	United States	Serial	Serial 0076 of Mozobil IND 55,851 - Protocol Amendment - New Investigator CV and 1572 Forms for	IND
95	15 Aug 2002	Mozobil	United States	Serial	Serial 0077 of Mozobil IND 55,851 - Safety Report	IND
96	27 Aug 2002	Mozobil	United States	Serial	Serial 0078 of Mozobil IND 55,851 - Protocol Amendment - New Investigator CV and 1572 Forms for	IND
97	13 Sep 2002	Mozobil	United States	Serial	Serial 0079 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 9 to Protocol 1003	IND
98	01 Oct 2002	Mozobil	United States	Serial	Serial 0080 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 1004	IND
99	03 Oct 2002	Mozobil	United States	Serial	Serial 0081 for Mozobil IND 55,851 - Other - Revised Investigator's Brochure	IND

100	18 Oct 2002	Mozobil	United States	Serial	Serial 0082 to Mozobil IND 55,851 - Protocol Amendment Change in Protocol - Amendment Number 1 to Protocol 2101	IND
101	24 Oct 2002	Mozobil	United States	Serial	Serial 0083 to Mozobil IND 55,851 - Protocol Amendment New Investigator - CV and 1572 Form for	IND
102	13 Nov 2002	Mozobil	United States	Serial	Serial 0084 of Mozobil IND 55,851 - Protocol Amendment New Investigator - CV and 1572 Form for	IND
103	15 Nov 2002	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. Annual Registration of Foreign Non-US Establishments	IND
104	22 Nov 2002	Mozobil	United States	Serial	Serial 0085 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 2 to Protocol 2101	IND
105	04 Dec 2002	Mozobil	United States	Serial	Serial 0086 of Mozobil IND 55,851 - Information Amendment Chemistry Microbiology - Modifications of Assay for Drug Product and Drug Substance	IND
106	13 Dec 2002	Mozobil	United States	Serial	Serial 0087 of Mozobil IND 55,851 - Protocol Amendment Change in Protocol - Amendment Number 10 to Protocol 1003	IND
107	17 Jan 2003	Mozobil	United States	Serial	Serial 0088 of Mozobil IND 55,851 - Potocol Amendment - New Protocol AMD3100-2102	IND
108	20 Jan 2003	Mozobil	United States	Serial	Serial 0089 of Mozobil IND 55,851 - Protocol Amendment New Investigator - CV and 1572 Form for	IND
109	27 Jan 2003	Mozobil	United States	Serial	Serial 0090 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 1004	IND
110	30 Jan 2003	Mozobil	United States	Application	Application for Orphan Drug Designation for Mozobil Submitted on 31 January 2003.	ODD
111	05 Feb 2003	Mozobil	United States	Serial	Serial 0091 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 1004	IND
112	06 Feb 2003	Mozobil	United States	Serial	Serial 0092 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 1004	IND
113	19 Feb 2003	Mozobil	United States	Serial	Serial 0093 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 1004	IND
114	27 Feb 2003	Mozobil	United States	Correspondence Received	Correspondence received acknowledgement of receipt of Mozobil ODD 03-1679 application.	ODD
115	28 Feb 2003	Mozobil	United States	Serial	Serial 0094 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Nimber 5 to Protocol 1005	IND
116	03 Mar 2003	Mozobil	United States	Serial	Serial 0095 of Mozobil IND 55,851 - Protocol Amendment - New Investigator CV and FDA Form 1572 for	IND
117	05 Mar 2003	Mozobil	United States	Serial	Serial 0096 of Mozobil IND 55,851 - Information Amendment - Pharmacology/Toxicology Final Study Reports and Summaries with Appendices	IND

118	12 Mar 2003	Mozobil	United States	Serial	Serial 0097 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 3 to Protocol 2101	IND
119	13 Mar 2003	Mozobil	United States	Serial	Serial 0098 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 1 to Protocol 2102	IND
120	11 Apr 2003	Mozobil	United States	Serial	Serial 0099 of Mozobil IND 55,851 - Protocol Amendment - New Protocol AMD3100-2103	IND
121	14 Apr 2003	Mozobil	United States	Serial	Serial 0100 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 1004	IND
122	22 Apr 2003	Mozobil	United States	Serial	Serial 0101 for Mozobil IND 55,851 - Safety Report - Initial to Protocol 2101	IND
123	01 May 2003	Mozobil	United States	Application	USAN Application regarding IND 55, 851 for Mozobil.	IND
124	08 May 2003	Mozobil	United States	Serial	Serial 0102 to Mozobil IND 55,851 - Protocol Amendment New Investigator - CV and 1572 Form for	IND
125	13 May 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding ODD 03-1679 for Mozobil.	ODD
126	21 May 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
127	21 May 2003	Mozobil	United States	Amendment	Amendment to Mozobil ODD 03-1679	ODD
128	03 Jun 2003	Mozobil	United States	Serial	Serial 0103 to Mozobil IND 55,851 - Safety Report - Initial to Protocol 2101.	IND
129	11 Jun 2003	Mozobil	United States	Serial	Serial 0104 of Mozobil IND 55,851 - Other - General Correspondence	IND
130	18 Jun 2003	Mozobil	United States	Serial	Serial 0105 of Mozobil IND 55,851 - Protocol Amendments and Annual Report - New Protocol AMD3100-2104 Change in Protocol Amendment Number 4 to Protocol 2101 - New Investigator CV and 1572 Form for - Annual Report Covering Reporting Period From 1 May 2002 to 1 May 2003	IND
131	24 Jun 2003	Mozobil	United States	Serial	Serial 0106 of Mozobil IND 55,851 - Safety Report - Initial and Follow-up to Protocol 2101	IND
132	02 Jul 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding ODD 03-1679	ODD
133	10 Jul 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil	IND
134	15 Jul 2003	Mozobil	United States	Serial	Serial 0107 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial Report to Protocol 2101 - New Investigator CV and 1572 Form	IND
135	16 Jul 2003	Mozobil	United States	Correspondence Received	Letter received that provides approval of ODD application 03-1679 for Mozobil.	ODD
136	18 Jul 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55,851 for Mozobil.	IND
137	18 Jul 2003	Mozobil	United States	Serial	Serial 0108 of Mozobil IND 55,851 - Potocol Amendments - New Protocol AMD3100-SPU001 - New Investigator CV and 1572 Form for	IND

138	21 Jul 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
139	21 Jul 2003	Mozobil	United States	Serial	Serial 0109 of Mozobil IND 55,851 - Safety Report - Initial and Follow-up to Protocol 2101	IND
140	22 Jul 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
141	24 Jul 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. QUESTIONS AND ANSWERS REGARDING	IND
142	13 Aug 2003	Mozobil	United States	Serial	Serial 0110 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial to Protocol 2102 - New Investigators	IND
143	15 Aug 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
144	18 Aug 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
145	19 Aug 2003	Mozobil	United States	Correspondence Sent	Correspondence sent, questions regarding the Orphan Drug Grant Application for Mozobil ODD 03-1679.	ODD
146	29 Aug 2003	Mozobil	United States	Serial	Serial 0111 of Mozobil IND 55,851 - Other -	IND
147	29 Aug 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
148	02 Sep 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. Approval to Treat CUP Patient	IND
149	10 Sep 2003	Mozobil	United States	Serial	Serial 0112 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Follow-up to Protocol 2102 - Change in Protocol Amendments to Protocols 2101, 2103 and 2104	IND
150	10 Sep 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
151	17 Sep 2003	Mozobil	United States	Serial	Serial 0113 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 5 to Protocol AMD3100-1004	IND
152	26 Sep 2003	Mozobil	United States	Serial	Serial 0114 of Mozobil IND 55,851 - Safety Reports - Initial to Protocols SPU001 and 2101	IND

153	08 Oct 2003	Mozobil	United States	Serial	Serial 0115 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Follow-up to Protocol 2101 - Change in Protocol Amendment Number 2 to Protocol 2103	IND
154	14 Oct 2003	Mozobil	United States	Serial	Serial 0116 of Mozobil IND 55,851 - Other - Request for Single Patient Use for Patient in SPU001 Protocol	IND
155	14 Oct 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
156	14 Oct 2003	Mozobil	United States	Correspondence Sent	Correspondence sent, grant application for ODD 03-1679 for Mozobil.	ODD
157	14 Oct 2003	Mozobil	United States	Correspondence Sent	Correspondence sent, grant application for Mozobil ODD 03-1679 for clinical trial	ODD
158	16 Oct 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. RECEIPT OF FDA'S APPROVAL TO TREAT PATIENT (SERIAL 0116)	IND
159	17 Oct 2003	Mozobil	United States	Correspondence Received	Correspondence received	ODD
160	17 Oct 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	ODD
161	20 Oct 2003	Mozobil	United States	Serial	Serial 0117 of Mozobil IND 55,851 - Protocol Amendment and Other - Change in Protocol Amendment Number 2 to Protocol 2104 - Updated 1572 Forms for for Protocol 2103	IND
162	23 Oct 2003	Mozobil	United States	Serial	Serial 0118 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial to Protocol 2102 - New Protocol AMD3100-CUP001	IND
163	29 Oct 2003	Mozobil	United States	Serial	Serial 0119 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 2101	IND
164	03 Nov 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD

165	04 Nov 2003	Mozobil	United States	Serial	Serial 0120 of Mozobil IND 55,851 - Protocol Amendment - New Protocol AMD3100-2105	IND
166	12 Nov 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
167	18 Nov 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Comments Regarding Compassionate Use Program	IND
168	20 Nov 2003	Mozobil	United States	Serial	Serial 0121 for Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 6 to Protocol 1004	IND
169	21 Nov 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
170	28 Nov 2003	Mozobil	United States	Serial	Serial 0122 to Mozobil IND 55,851 - Other - Request for Compassionate Use for Patients in CUP001 Protocol	IND
171	28 Nov 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
172	01 Dec 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat 3 CUP Patients	IND
173	02 Dec 2003	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
174	04 Dec 2003	Mozobil	United States	Serial	Serial 0123 to Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 3 to Protocol 2103.	IND
175	05 Dec 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
176	15 Dec 2003	Mozobil	United States	Serial	Serial 0124 of Mozobil IND 55,851 - Other -	IND
177	15 Dec 2003	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND

178	19 Dec 2003	Mozobil	United States	Serial	Serial 0125 of Mozobil IND 55,851 - Other - Minutes From 18 December 2003 Teleconference Regarding Compassionate Use Protocol Meeting	IND
179	24 Dec 2003	Mozobil	United States	Serial	Serial 0126 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2102	IND
180	09 Jan 2004	Mozobil	United States	Serial	Serial 0127 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patients in CUP001 Protocol	IND
181	09 Jan 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
182	14 Jan 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat CUP Patients	IND
183	20 Jan 2004	Mozobil	United States	Serial	Serial 0128 of Mozobil IND 55,851 - Safety Report and Potocol Amendment and Other - Follow-up Report to Protocol 2102 - New Investigators - Investigator's Brochure.	IND
184	20 Jan 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. Confirmation of Secure Email Between AnorMED and CDER	IND
185	28 Jan 2004	Mozobil	United States	Serial	Serial 0129 of Mozobil IND 55,851 - Other - Request for Type C Meeting to Discuss Further Development of AMD3100	IND
186	28 Jan 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD
187	29 Jan 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
188	11 Feb 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	ODD
189	17 Feb 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
190	23 Feb 2004	Mozobil	United States	Serial	Serial 0130 of Mozobil IND 55,851 - Safety Report and Other - Initial to Protocol 2102 - Request for Compassionate Use for Patient in CUP001 Protocol	IND

191	23 Feb 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
192	24 Feb 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat CUP Patient and Request for Patient Serial 0130	IND
193	27 Feb 2004	Mozobil	United States	Serial	Serial 0131 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
194	27 Feb 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat CUP Patient and Request for Patient Serial 0131	IND
195	01 Mar 2004	Mozobil	United States	Serial	Serial 0132 of Mozobil IND 55,851 - Protocol Amendment and Other - Change in Protocol Amendments to Protocols 1004, 2101 and 2105 - Request for Compassionate Use for Patient in CUP001 Protocol	IND
196	03 Mar 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat CUP Patient and Request for Patient Serial 0132	IND
197	05 Mar 2004	Mozobil	United States	Serial	Serial 0133 of Mozobil IND 55,851 - Protoco Amendment - New Protocol AMD3100-2106	IND
198	08 Mar 2004	Mozobil	United States	Serial	Serial 0134 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patients in CUP001 Protocol	IND
199	08 Mar 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
200	08 Mar 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
201	09 Mar 2004	Mozobil	United States	Serial	Serial 0135 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patients in CUP001 Protocol	IND
202	10 Mar 2004	Mozobil	United States	Serial	Serial 0136 of Mozobil IND 55,851 - Response to FDA Request for Information and Other - Clarify Eligibility of Patients for Single Patient Use Protocol - Request for Compassionate Use for Patients in CUP001 Protocol	IND
203	11 Mar 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat 4 CUP Patients	IND
204	18 Mar 2004	Mozobil	United States	Serial	Serial 0137 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patients in CUP001 Protocol	IND
205	18 Mar 2004	Mozobil	United States	Serial	Serial 0138 of Mozobil IND 55,851 - Other - Information Package for 7 April 2004 Type C Clinical Update Meeting	IND

206	18 Mar 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat CUP Patient	IND
207	19 Mar 2004	Mozobil	United States	Correspondence Sent	Correspondence Sent Regarding IND 55,851 for Mozobil.	IND
208	23 Mar 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
209	25 Mar 2004	Mozobil	United States	Serial	Serial 0139 of Mozobil IND 55,851 - Safety Report - Protocol Amendment and Other - Follow-up Report to Protocol 2102 - Amendment Number 4 to Protocol 2103 - Questions for Type C Clinical Update Meeting on 7 April 2003	IND
210	02 Apr 2004	Mozobil	United States	Serial	Serial 0140 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
211	05 Apr 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat CUP Patient	IND
212	05 Apr 2004	Mozobil	United States	Correspondence Sent	GRANT APPLICATION SENT REGARDING IND 55,851 FOR MOZOBIL.	ODD
213	05 Apr 2004	Mozobil	United States	Correspondence Sent	GRANT APPLICATION SENT REGARDING IND 55,851 FOR MOZOBIL.	ODD
214	06 Apr 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
215	07 Apr 2004	Mozobil	United States	Serial	Serial 0141 for Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
216	07 Apr 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
217	08 Apr 2004	Mozobil	United States	Serial	Serial 0142 to Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
218	09 Apr 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat CUP Patient	IND
219	12 Apr 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Approval to Treat CUP Patient	IND

220	15 Apr 2004	Mozobil	United States	Serial	Serial 0143 to Mozobil IND 55,851 - Protocol Amendments - Change in Protocol and New Investigator - Amendment Number 2 to Protocol 2102 and Curriculum Vitae and 1572 Forms for 8 New Investigators.	IND
221	19 Apr 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil.	IND
222	21 Apr 2004	Mozobil	United States	Serial	Serial 0144 of Mozobil IND 55,851 - Information Amendment - Pharmacology Toxicology - Clinical Pharmacology and Biopharmaceutics Plan	IND
223	22 Apr 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
224	26 Apr 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD
225	26 Apr 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD
226	27 Apr 2004	Mozobil	United States	Serial	Serial 0145 of Mozobil IND 55,851 - Other - AnorMED Minutes From 7 April 2007 Type C Clinical Update Meeting	IND
227	28 Apr 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
228	28 Apr 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD
229	29 Apr 2004	Mozobil	United States	Serial	Serial 0146 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2104 and Follow-up to Protocol 2101	IND
230	29 Apr 2004	Mozobil	United States	Serial	Serial 0147 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
231	03 May 2004	Mozobil	United States	Serial	Serial 0148 of Mozobil IND 55,851 - Potocol Amendment - Change in Protocol Amendment Number 3 to Protocol 2104	IND
232	03 May 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA Official Meeting Minutes From April 7 End of Phase I	IND
233	04 May 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. Approval to Treat CUP Patient	IND

234	05 May 2004	Mozobil	United States	Serial	Serial 0149 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
235	05 May 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD
236	06 May 2004	Mozobil	United States	Serial	Serial 0150 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2101	IND
237	06 May 2004	Mozobil	United States	Serial	Serial 0151 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
238	06 May 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
239	07 May 2004	Mozobil	United States	Serial	Serial 0152 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
240	09 May 2004	Mozobil	United States	Correspondence Received	Correspondence Received regarding IND 55, 851 for Mozobil.	IND
241	10 May 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
242	18 May 2004	Mozobil	United States	Serial	Serial 0153 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2102	IND
243	20 May 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
244	21 May 2004	Mozobil	United States	Serial	Serial 0154 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patients in CUP001 Protocol	IND
245	24 May 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
246	24 May 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	ODD

247	25 May 2004	Mozobil	United States	Serial	Serial 0155 of Mozobil IND 55,851 - Other - Request for Comment on Phase III Concept Sheets	IND
248	25 May 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
249	25 May 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
250	26 May 2004	Mozobil	United States	Contact Report	Bem Atsma contacted Ann Staten at FDA to discuss the procedure of Special Protocol Assessments	IND
251	02 Jun 2004	Mozobil	United States	Serial	Serial 0156 of Mozobil IND 55,851 - Safety Report - Protocol Amendment - Initial Report to Protocol 2103 - New Investigator Revised FDA 1572 Forms for 3 Investigators	IND
252	02 Jun 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
253	03 Jun 2004	Mozobil	United States	Serial	Serial 0157 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
254	03 Jun 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
255	07 Jun 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
256	09 Jun 2004	Mozobil	United States	Serial	Serial 0158 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
257	10 Jun 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
258	10 Jun 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
259	10 Jun 2004	Mozobil	United States	Contact Report	Bem Atsma contacted Janet Whitely and Henry Startsman at OPD regarding reviewers comments to our grant application	ODD
260	15 Jun 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
261	17 Jun 2004	Mozobil	United States	Serial	Serial 0159 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND

262	18 Jun 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
263	22 Jun 2004	Mozobil	United States	Serial	Serial 0160 of Mozobil IND 55,851 - Safety Report - Protocol Amendment Change in Protocol - Initial Report to Protocol CUP001 - Amendment Number 5 to Protocol 2103 and Amendment Number 2 to Protocol 2105	IND
264	24 Jun 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
265	28 Jun 2004	Mozobil	United States	Serial	Serial 0161 for Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 4 to Protocol 2104	IND
266	30 Jun 2004	Mozobil	United States	Serial	Serial 0162 to Mozobil IND 55,851 - Safety Report and Annual Report - Initial to Protocols 1004, 2104 and 2105 and Follow-up to Protocol 2103 - Annual Report to Cover Period From 1 May 2003 - 5 May 2004	IND
267	06 Jul 2004	Mozobil	United States	Serial	Serial 0163 to Mozobil IND 55,851 - Safety Report - Protocol Amendments - New Protocol and New Investigator - Initial Report to Protocol 2105 and Follow-up Reports to Protocols 1004, 2105 and CUP - New Protocol AMD3100-2107 and Curriculum Vitae and 1572 Forms for 4 New Investigators.	IND
268	06 Jul 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
269	12 Jul 2004	Mozobil	United States	Serial	Serial 0164 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2104	IND
270	14 Jul 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
271	15 Jul 2004	Mozobil	United States	Serial	Serial 0165 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
272	15 Jul 2004	Mozobil	United States	Contact Report	Bem Atsma contacted Ann Staten at FDA for an update on the Phase III concept sheet review	IND
273	16 Jul 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
274	16 Jul 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND

275	19 Jul 2004	Mozobil	United States	Serial	Serial 0166 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
276	19 Jul 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
277	20 Jul 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
278	20 Jul 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
279	21 Jul 2004	Mozobil	United States	Serial	Serial 0167 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol Amendment Number 3 to Protocol 2105	IND
280	23 Jul 2004	Mozobil	United States	Serial	Serial 0168 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
281	27 Jul 2004	Mozobil	United States	Correspondence Received	Correspondence Received regarding IND 55, 851 for Mozobil.	IND
282	28 Jul 2004	Mozobil	United States	Serial	Serial 0169 of Mozobil IND 55,851 - Other - End of Phase II Meeting Request	IND
283	30 Jul 2004	Mozobil	United States	Serial	Serial 0170 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 2103, 2104 and CUP001	IND
284	30 Jul 2004	Mozobil	United States	Serial	Serial 0171 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
285	30 Jul 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD
286	03 Aug 2004	Mozobil	United States	Serial	Serial 0172 of Mozobil IND 55,851 - Protocol Amendments - New Protocol 2108 and New Investigator and Revised 1572 Form for	IND
287	03 Aug 2004	Mozobil	United States	Serial	Serial 0173 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
288	03 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
289	04 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil that provides approval to treat PATIENT	IND

290	04 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
291	04 Aug 2004	Mozobil	United States	Contact Report	Bem Atsma called Jeff Fritsch at OOPD confirming their involvement in the End of Phase II Meeting with CDER	ODD
292	06 Aug 2004	Mozobil	United States	Serial	Serial 0174 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patients in CUP001 Protocol	IND
293	09 Aug 2004	Mozobil	United States	Serial	Serial 0175 of Mozobil IND 55,851 - Safety Report - Initial Nonclinical -	IND
294	10 Aug 2004	Mozobil	United States	Serial	Serial 0176 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
295	10 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. REQUEST TO TREAT PATIIENT #019-001 WAS SENT AND APPROVAL RECEIVED. SERIAL #174.	IND
296	11 Aug 2004	Mozobil	United States	Serial	Serial 0177 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
297	11 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. REQUEST TO TREAT PATIENT WAS SENT AND APPROVAL RECEIVED. SERIAL #176.	IND
298	12 Aug 2004	Mozobil	United States	Serial	Serial 0178 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2102	IND
299	12 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. REQUEST TO TREAT PATIENT WAS SENT AND APPROVAL RECEIVED. SERIAL #177.	IND
300	13 Aug 2004	Mozobil	United States	Serial	Serial 0179 of Mozobil IND 55,851 - Other - Information Package for End of Phase II Meeting	IND
301	13 Aug 2004	Mozobil	United States	Serial	Serial 0180 of Mozobil IND 55,851 - Other - Request for Compassionate Use for Patient in CUP001 Protocol	IND
302	16 Aug 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. END OF PHASE II MEETING PACKAGE WAS SENT TO FDA AND PROTOCOL SYNOPSES ELECTRONICALLY.	IND
303	16 Aug 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD
304	17 Aug 2004	Mozobil	United States	Serial	Serial 0181 for Mozobil IND 55,851 - Safety Report and Other - Initial reports to Protocols 2103, 2105 and CUP001 and Follow-up to Protocol 2103 - Request for Single Patient Exemption	IND

305	17 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. REQUEST TO TREAT PATIENT WAS SENT AND APPROVAL RECEIVED. SERIAL #180.	IND
306	19 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. REQUEST TO TREAT PATIENT WAS SENT AND APPROVAL RECEIVED. SERIAL #181	IND
307	25 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	ODD
308	27 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil.	IND
309	30 Aug 2004	Mozobil	United States	Serial	Serial 0182 to Mozobil IND 55,851 - Safety Report and Other - Initial to Protocol 2105 - Enrollment into CUP001 Protocol for Patients	IND
310	31 Aug 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
311	02 Sep 2004	Mozobil	United States	Serial	Serial 0183 to Mozobil IND 55,851 - Other - Request for Compassionate Use - Response to FDA Request for Information for End of Phase II - Enroll Patients into CUP001 Protocol	IND
312	02 Sep 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
313	03 Sep 2004	Mozobil	United States	Serial	Serial 0184 of Mozobil IND 55,851 - Protocol Amendment - New Protocol and Information Amendment - Pharmacology/Toxicology. Amendment Number 5 to Protocol 2104.	IND
314	07 Sep 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND

315	07 Sep 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. REQUEST TO TREAT PATIENTS UNDER CARE OF APPROVAL TO TREAT THESE PATIENTS RECEIVED SEPTEMBER 7TH (DELAY DUE TO PROBLEM WITH FDA NOT RECEIVING FAX UNTIL SEPTEMBER 3RD).	IND
316	08 Sep 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. ANORMED'S RESPONSES TO INITIAL FDA COMMENTS FROM THEIR INTERNAL PRE-MEETING. FULL SECTIONS FROM PHASE III PROTOCOL ARE INCLUDED	IND
317	10 Sep 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
318	13 Sep 2004	Mozobil	United States	Serial	Serial 0185 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocols 2104 and 2105	IND
319	15 Sep 2004	Mozobil	United States	Serial	Serial 0186 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 2104 and 2105	IND
320	17 Sep 2004	Mozobil	United States	Annual Report	Annual Report for Mozobil ODD 03-1679 covering the reporting reporting period 01 Jan 2003 through 17 Sep 2004.	ODD
321	17 Sep 2004	Mozobil	United States	Serial	Serial 0187 of Mozobil IND 55,851 - Other - Request for Special Protocol Assessment 3101	IND
322	17 Sep 2004	Mozobil	United States	Serial	Serial 0188 of Mozobil IND 55,851 - Other - Request for Special Protocol Assessment 3102	IND
323	20 Sep 2004	Mozobil	United States	Serial	Serial 0189 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocols 2103 and CUP001	IND
324	20 Sep 2004	Mozobil	United States	Serial	Serial 0190 of Mozobil IND 55,851 - Other - Request for CMC End of Phase II Meeting for AMD3100	IND
325	20 Sep 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
326	20 Sep 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. COPY OF SERIAL #190 SENT TO ANN TO REQUEST A CMC END OF PHASE II MEETING WITH THE AGENCY.	IND
327	24 Sep 2004	Mozobil	United States	Serial	Serial 0191 of Mozobil IND 55,851 - Other - Compassionate Use Update -	IND

328	27 Sep 2004	Mozobil	United States	Correspondence Received	Correspondence Received regarding IND 55,851 for Mozobil.	IND
329	27 Sep 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil. CMC EOPII TELECONFERENCE HAS BEEN SET FOR NOVEMBER 17/04 AT 1PM EST.	IND
330	30 Sep 2004	Mozobil	United States	Serial	Serial 0192 of Mozobil IND 55,851 - Protocol Amendments - New Protocol 2103 and New Investigator	IND
331	30 Sep 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil.	IND
332	01 Oct 2004	Mozobil	United States	Serial	Serial 0193 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 2105	IND
333	05 Oct 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil. OFFICIAL FDA MINUTES RECEIVED FOR THE END OF PHASE II MEETING HELD ON SEPT 10/04	IND
334	06 Oct 2004	Mozobil	United States	Correspondence Sent	GRANT APPLICATION SENT REGARDING IND 55,851 FOR MOZOBIL. RFA-FDA-OPD-2005-1 RE-SUBMISSION OF PROTOCOL 2106 - PATIENTS WITH HODGKIN'S DISEASE. SUMMARY STATEMENT RD-R-02591-01	ODD
335	07 Oct 2004	Mozobil	United States	Serial	Serial 0194 of Mozobil IND 55,851 - Protocol Amendment Change in Protocol - Amendment Number 3 for Protocol 2102	IND
336	08 Oct 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil. RECEIVED FROM CYNTHIA POLIT STATING THAT OUR SUBMISSION OF PROTOCOL AMD3100-2106 HAD BEEN RECEIVED TODAY. THE APPLICATION NUMBER ASSIGNED IS 1R01 FD003010-01	ODD
337	12 Oct 2004	Mozobil	United States	Serial	Serial 0195 of Mozobil IND 55,851 - Safety Report - Initial Reports to Protocols 2105 and CUP001	IND
338	13 Oct 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil.	IND

339	14 Oct 2004	Mozobil	United States	Serial	Serial 0196 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial to Protocol 2104 - Change in Protocol Amendment Number 1 to Protocol 2108	IND
340	15 Oct 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. Grant Application for Protocol 2106 has been assigned 1 R01 FD003010-01	ODD
341	19 Oct 2004	Mozobil	United States	Serial	Serial 0197 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2105 and Follow-uup to Protocol 2103	IND
342	21 Oct 2004	Mozobil	United States	Serial	Serial 0198 of Mozobil IND 55,851 - Other - CMC End of Phase II Information Package	IND
343	22 Oct 2004	Mozobil	United States	Serial	Serial 0199 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001	IND
344	26 Oct 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. INFORMED FDA THAT CMC EOPII PACKAGE WAS SHIPPED.	IND
345	02 Nov 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
346	04 Nov 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. TING TO BE HELD ON WEDNESDAY 10TH NOVEMBER AND COMMENTS WILL BE RECEIVED BY FRIDAY 12TH NOVEMBER	IND
347	08 Nov 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
348	10 Nov 2004	Mozobil	United States	Serial	Serial 0200 of Mozobil IND 55,851 - Protocol Amendment - New Investigator - Approval of Multiple Investigators	IND
349	10 Nov 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA ANSWERS TO QUESTIONS	IND
350	10 Nov 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
351	10 Nov 2004	Mozobil	United States	Contact Report	Teleconference with Ann Staten and Ann Farrel from FDA and Gary Calandra and Bem Atsma regarding SPA on Phase III Protocols	IND
352	15 Nov 2004	Mozobil	United States	Serial	Serial 0201 for Mozobil IND 55,851 - Protocol Amendment - Change In Protocol - Amendments to 3101 and 3102	IND
353	15 Nov 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. SPA QUESTIONS LIST SENT TO ANN STATEN ELECTRONICALLY	IND

354	15 Nov 2004	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. AMENDMENTS TO PROTOCOLS AMD3100-3101 AND 3102 (SERIAL #201)	IND
355	16 Nov 2004	Mozobil	United States	Contact Report	Bem Atsma contacted Ann Staten at FDA regarding cancellation of End of Phase II CMC Meeting	IND
356	19 Nov 2004	Mozobil	United States	Serial	Serial 0202 to Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2104	IND
357	22 Nov 2004	Mozobil	United States	Serial	Serial 0203 to Mozobil IND 55,851 - Safety Report and Other - Initial to Protocols 2103, 2104, 2105 and CUP001 - CMC Comments	IND
358	24 Nov 2004	Mozobil	United States	Serial	Serial 0204 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 2104, 2105 and CUP001	IND
359	30 Nov 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. AGENCYS SPA LETTERS FROM ANN STATEN	IND
360	01 Dec 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. OFFICIAL FDA MINUTES RECEIVED FOR THE CMC END OF PHASE II MEETING REQUEST	IND
361	02 Dec 2004	Mozobil	United States	Serial	Serial 0205 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial Report to Protocols 2103 and 2104 - Change In Protocol Amendment Number 2 to Protocols 3101 and 3102	IND
362	02 Dec 2004	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. CONFIRMATION FROM FDA	IND
363	09 Dec 2004	Mozobil	United States	Serial	Serial 0206 of Mozobil IND 55,851 - Other - Request for Single Patient Exemption - Sister 1 and Sister 2	IND
364	09 Dec 2004	Mozobil	United States	Correspondence Sent	Correspondence sent IND 55, 851 for Mozobil. COPY OF SERIAL #206 WAS FAXED TO REQUEST SINGLE PATIENT EXCEPTION FOR PROTOCOL CUP-001, CARE OF	IND
365	10 Dec 2004	Mozobil	United States	Serial	Serial 0207 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial Report to Protocol 2104 and Follow-up to Protocol 2103 - Change in Protocol Amendments to Protocols 2101 and 2104 - Four New Investigators	IND
366	16 Dec 2004	Mozobil	United States	Serial	Serial 0208 of Mozobil IND 55,851 - Safety Report and General Correspondence - Follow-up to Protocol 2103 - Request for Single Patient Exemption	IND
367	20 Dec 2004	Mozobil	United States	Serial	Serial 0209 of Mozobil IND 55,851 - Safety Report and Other - Initial Report to Protocols 2104 and CUP001 - Brand Name Proposal	IND
368	22 Dec 2004	Mozobil	United States	Serial	Serial 0210 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 2103 and 2105 - Follow-up to Protocol 2104	IND
369	05 Jan 2005	Mozobil	United States	Serial	Serial 0211 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2104	IND
370	07 Jan 2005	Mozobil	United States	Serial	Serial 0212 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001	IND

371	07 Jan 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. CUP001 SAE REPORT	IND
372	11 Jan 2005	Mozobil	United States	Serial	Serial 0213 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 2104	IND
373	17 Jan 2005	Mozobil	United States	Correspondence Received	Correspondence Received regarding IND 55, 851 for Mozobil.	IND
374	17 Jan 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. AMENDMENT ENQUIRY FOR CUP001	IND
375	24 Jan 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. NOTIFICATION OF CHANGE OF DATE FOR NIH COUNCIL, TO BE IN MAY 2005 (PROTOCOL 2106 (HD)	ODD
376	04 Feb 2005	Mozobil	United States	Serial	Serial 0214 of Mozobil IND 55,851 - Protocol Amendment Change in Protocol and Protocol Amendment New Investigator - Amendments for Protocols 3101 and 3102 - Four New Investigators	IND
377	11 Feb 2005	Mozobil	United States	Serial	Serial 0215 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocols 2104 and 2105	IND
378	16 Feb 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.ENQUIRY ABOUT OUR BRAND NAME PROPOSAL.	IND
379	17 Feb 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FOLLOW-UP TO A QUESTION	IND
380	21 Feb 2005	Mozobil	United States	Serial	Serial 0216 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2105	IND
381	24 Feb 2005	Mozobil	United States	Serial	Serial 0217 of Mozobil IND 55,851 - Safety Report - Initial to Protocol C201	IND
382	24 Feb 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. ANN LEFT MESSAGE TO GET UPDATE ON CUP PATIENT DETAILS FROM SERIAL NO. 206 AND 208.	IND
383	28 Feb 2005	Mozobil	United States	Serial	Serial 0218 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial to Protocol 2104 - Four New Investigators	IND
384	03 Mar 2005	Mozobil	United States	Serial	Serial 0219 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2105 and Follow-up to Protocol 2104 - Protocol Amendment New Protocol AMD3100-2104 - Change In Protocol Amendments to Protocols 2106 2108, 2109 and CUP001	IND

385	03 Mar 2005	Mozobil	United States	Serial	Serial 0220 of Mozobil IND 55,851 - General Correspondence -	IND
386	03 Mar 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. COPY OF SERIAL #220	IND
387	07 Mar 2005	Mozobil	United States	Serial	Serial 0221 for Mozobil IND 55,851 - Information Amendment - Pharmacology Toxicology Multiple Studies I	IND
388	08 Mar 2005	Mozobil	United States	Serial	Serial 0222 to Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101 - Follow-up to Protocol 2105	IND
389	09 Mar 2005	Mozobil	United States	Serial	Serial 0223 to Mozobil IND 55,851 - Other - Written Request for AMD3100 Pediatric Study	IND
390	10 Mar 2005	Mozobil	United States	Serial	Serial 0224 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2104	IND
391	10 Mar 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
392	11 Mar 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
393	15 Mar 2005	Mozobil	United States	Serial	Serial 0225 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocols 2104 and Corrected 2105	IND
394	17 Mar 2005	Mozobil	United States	Serial	Serial 0226 of Mozobil IND 55,851 - Protocol Amendment - Change in Protocol -	IND
395	17 Mar 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	ODD
396	22 Mar 2005	Mozobil	United States	Serial	Serial 0227 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol C201 and Follow-up to Protocol 2105	IND
397	29 Mar 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
398	30 Mar 2005	Mozobil	United States	Serial	Serial 0228 of Mozobil IND 55,851 - Other - Phase III Statistical Analysis Plans Protocols 3101 and 3102	IND
399	31 Mar 2005	Mozobil	United States	Serial	Serial 0229 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 2105	IND
400	31 Mar 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
401	04 Apr 2005	Mozobil	United States	Serial	Serial 0230 of Mozobil IND 55,851 - Protocol Amendment - New Investigator - Eight New Investigators	IND

402	05 Apr 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	ODD
403	07 Apr 2005	Mozobil	United States	Serial	Serial 0231 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001 and Follow-up to Protocol 2105	IND
404	12 Apr 2005	Mozobil	United States	Serial	Serial 0232 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial to Protocol 2102 - New Protocol AMD3100-2112	IND
405	13 Apr 2005	Mozobil	United States	Serial	Serial 0233 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocols CUP001 and Corrected 2102	IND
406	15 Apr 2005	Mozobil	United States	Serial	Serial 0234 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001 - Follow-up to Protocol 2102	IND
407	15 Apr 2005	Mozobil	United States	Correspondence Sent	GRANT APPLICATION SENT REGARDING IND 55,851 FOR MOZOBIL. NUMBER RFA-FDA-OPD-2006 FOR PROTOCOL AMD3100-3102 AMENDMENTS #1,#2 AND #3. SPECIAL PROTOCOL ASSESSMENT REQUEST AND FDA RESPONSE DRAFT INFORMED CONSENT FORM	ODD
408	18 Apr 2005	Mozobil	United States	Serial	Serial 0235 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol CUP001	IND
409	20 Apr 2005	Mozobil	United States	Serial	Serial 0236 of Mozobil IND 55,851 - Safety Report - Initial and Follow-up to Protocol CUP001	IND
410	21 Apr 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. CONFIRMING GRANT APPLICATION HAS BEEN RECEIVED. NUMBER ASSIGNED TO APPLICATION 1R01 FD003104-01	ODD
411	25 Apr 2005	Mozobil	United States	Serial	Serial 0237 of Mozobil IND 55,851 - Safety Report - Initial to Protocols C201 and 3102 and Follow-up to Protocol CUP001	IND
412	27 Apr 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. ORPHAN GRANT APPLICATION FOR PROTOCOL 2106 (HD) SECOND REVIEW OF 2106 GRANT APPLICATION	ODD
413	29 Apr 2005	Mozobil	United States	Serial	Serial 0238 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial to Protocol CUP001 - Six New Investigators	IND
414	05 May 2005	Mozobil	United States	Serial	Serial 0239 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102	IND
415	10 May 2005	Mozobil	United States	Serial	Serial 0240 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2105 and 3102	IND
416	12 May 2005	Mozobil	United States	Serial	Serial 0241 for Mozobil IND 55,851 - Safety Reports - Other - Follow-up to 2105 Protocol Annotations and Changes to Protocols 3101 and 3102	IND
417	19 May 2005	Mozobil	United States	Serial	Serial 0242 to Mozobil IND 55,851 - Safety Report - Initial to Protocols 2103 and 2109 - Follow-up to Protocols 3102 and CUP001	IND

418	19 May 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
419	26 May 2005	Mozobil	United States	Serial	Serial 0243 to Mozobil IND 55,851 - Safety Report - Protocol Amendment New Protocol - Initial Report to Protocol 2104 and Follow-up to Protocol CUP001 - New Protocol Submitted 2113	IND
420	31 May 2005	Mozobil	United States	Serial	Serial 0244 of Mozobil IND 55,851 - Safety Report - Protocol Amendment - Initial to Protocol CUP001 - Five New Investigators.	IND
421	01 Jun 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA comments regarding the SAPs for Phase III	IND
422	06 Jun 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
423	07 Jun 2005	Mozobil	United States	Serial	Serial 0245 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - New Investigator - Initial Report to Protocol 2104 and Follow-up to Protocols C201, CUP001 and 2104 - Two New Investigators	IND
424	08 Jun 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. QUESTIONS TO DETERMINE PROCEDURES	IND
425	10 Jun 2005	Mozobil	United States	Serial	Serial 0246 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial Report to Protocol 2105 - Change in Protocol Amendment Number 2 to Protocol 2106	IND
426	13 Jun 2005	Mozobil	United States	Serial	Serial 0247 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol CUP001	IND
427	15 Jun 2005	Mozobil	United States	Serial	Serial 0248 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocols EU21 and 3101	IND
428	15 Jun 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND

429	16 Jun 2005	Mozobil	United States	Serial	Serial 0249 of Mozobil IND 55,851 - Safety Report and Response to FDA Request for Information - Initial Report to Protocol 3101 and Follow-up to Protocol CUP001 - DSMB Charters	IND
430	17 Jun 2005	Mozobil	United States	Serial	Serial 0250 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001	IND
431	21 Jun 2005	Mozobil	United States	Serial	Serial 0251 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 2105 and CUP001	IND
432	27 Jun 2005	Mozobil	United States	Serial	Serial 0252 of Mozobil IND 55,851 - Safety Report and Annual Report - Initial to Protocols 2105 and CUP001 - Follow-up to Protocol 3101 - Annual Report Covering the Reporting Period From 6 May 2004 to 5 May 2005	IND
433	29 Jun 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
434	30 Jun 2005	Mozobil	United States	Serial	Serial 0253 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol C201	IND
435	04 Jul 2005	Mozobil	United States	Serial	Serial 0254 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001 - Follow-up to Protocol C201	IND
436	05 Jul 2005	Mozobil	United States	Serial	Serial 0255 of Mozobil IND 55,851 - Protocol Amendment - New Investigator Twelve New Investigators	IND
437	06 Jul 2005	Mozobil	United States	Serial	Serial 0256 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 2104 - Follow-up to Protocol CUP001	IND
438	08 Jul 2005	Mozobil	United States	Serial	Serial 0257 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial to Protocol 2104 and Follow-up to Protocol C201 - Change in Protocol Amendments to Protocols 3101 and 3102	IND
439	11 Jul 2005	Mozobil	United States	Contact Report	Bem Atsma called Ann Staten at FDA to ask a series of questions:	IND
440	12 Jul 2005	Mozobil	United States	Serial	Serial 0258 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2105	IND
441	13 Jul 2005	Mozobil	United States	Serial	Serial 0259 of Mozobil IND 55,851 - Safety Report - Initial to Protocols C201 and 3102 - Follow-up to Protocol 3102	IND
442	14 Jul 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
443	15 Jul 2005	Mozobil	United States	Serial	Serial 0260 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Initial to Protocols 3101 and CUP001 - Follow-up to Protocol 2105 - New Protocol AMD3100-1101	IND
444	20 Jul 2005	Mozobil	United States	Serial	Serial 0261 for Mozobil IND 55,851 - Safety Reports - Initial to 2109 Protocol	IND
445	22 Jul 2005	Mozobil	United States	Serial	Serial 0262 to Mozobil IND 55,851 - Safety Report - Initial to Protocol 2104 - Follow-up to Protocols 2104 and CUP001	IND

446	25 Jul 2005	Mozobil	United States	Serial	Serial 0263 to Mozobil IND 55,851 - Safety Report - Initial to Protocol 2104	IND
447	27 Jul 2005	Mozobil	United States	Serial	Serial 0264 of Mozobil IND 55,851 - Safety Report - Initial to Protocols EU21, 2104 and CUP001and Follow-up to Protocols 2104 and CUP001.	IND
448	29 Jul 2005	Mozobil	United States	Serial	Serial 0265 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - New Investigator - Initial Report to Protocol EU21 - Six New Investigators	IND
449	03 Aug 2005	Mozobil	United States	Serial	Serial 0266 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol CUP001	IND
450	05 Aug 2005	Mozobil	United States	Serial	Serial 0267 of Mozobil IND 55,851 - Safety Report - Initial and Follow-up Reports to Protocol 3101	IND
451	08 Aug 2005	Mozobil	United States	Serial	Serial 0268 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Change in Protocol - Initial Report to Protocol 2102 - Amendment Number 5 to Protocol 3101 and Amendment Number 6 to Protocol 3102	IND
452	10 Aug 2005	Mozobil	United States	Serial	Serial 0269 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 2104	IND
453	12 Aug 2005	Mozobil	United States	Serial	Serial 0270 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 2105, 3101 and CUP001	IND
454	19 Aug 2005	Mozobil	United States	Serial	Serial 0271 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and 3101	IND
455	31 Aug 2005	Mozobil	United States	Serial	Serial 0272 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101	IND
456	02 Sep 2005	Mozobil	United States	Serial	Serial 0273 of Mozobil IND 55,851 - Safety Report - Initial and follow-up Reports to Protocol CUP001	IND
457	06 Sep 2005	Mozobil	United States	Correspondence Received	Correspondence RECEIVED regarding IND 55, 851 for Mozobil.	IND
458	07 Sep 2005	Mozobil	United States	Serial	Serial 0274 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 2102 and CUP001 - Follow-up to Protocol 3101	IND
459	09 Sep 2005	Mozobil	United States	Serial	Serial 0275 of Mozobil IND 55,851 - Safety Report and Protocol Amendment - Change in Protocol - Initial Report to Prootcol 3102 - Amendment Number 6 to Protocol 3101 and Amendment Number 7 to Protocol 3102	IND
460	12 Sep 2005	Mozobil	United States	Serial	Serial 0276 of Mozobil IND 55,851 - Safety Report - Information Amendment Clinical - Protocol Amendment New Investigator - Initial Report to Protocol 3102 - Clinical Data Use - Eleven New Investigators	IND
461	15 Sep 2005	Mozobil	United States	Serial	Serial 0277 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and C201	IND
462	19 Sep 2005	Mozobil	United States	Serial	Serial 0278 of Mozobil IND 55,851 - Safety Report and Protocol Amendment Change in Protocol - Initial to Protocol 3101 - Follow-up to Protocol 3102 - Amendment Number 3 to Protocol 2106	IND

463	21 Sep 2005	Mozobil	United States	Serial	Serial 0279 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocols C201 and 2104	IND
464	23 Sep 2005	Mozobil	United States	Serial	Serial 0280 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and CUP001	IND
465	26 Sep 2005	Mozobil	United States	Serial	Serial 0281 for Mozobil IND 55,851 - Safety Reports - Initial to Protocol CUP001 - Follow-up to Protocol 2103	IND
466	28 Sep 2005	Mozobil	United States	Serial	Serial 0282 to Mozobil IND 55,851 - Safety Report and Protocol Amendment: Change in Protocol 3101 Amendment 7 and Amendment 8 to Protocol 3102 - Initial Report to Protocol CUP001	IND
467	29 Sep 2005	Mozobil	United States	Serial	Serial 0283 to Mozobil IND 55,851 - Other - CUP Enrollment for Patient	IND
468	29 Sep 2005	Mozobil	United States	Serial	Serial 0284 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101 and Follow-up to Protocol 3102.	IND
469	30 Sep 2005	Mozobil	United States	Correspondence Received	Correspondence Received regarding IND 55,851 for Mozobil. COMPASSIONATE USE REQUEST FAXED TO AGENCY SERIAL #0283.	IND
470	04 Oct 2005	Mozobil	United States	Serial	Serial 0285 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and CUP001	IND
471	04 Oct 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55,851 for Mozobil.	ODD
472	06 Oct 2005	Mozobil	United States	Serial	Serial 0286 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 3101	IND
473	07 Oct 2005	Mozobil	United States	Annual Report	Annual Report for Mozobil ODD 03-1679 covering the reporting period 10 Sep 2004 through 10 Sep 2005.	ODD
474	07 Oct 2005	Mozobil	United States	Serial	Serial 0287 of Mozobil IND 55,851 - Protocol Amendment - New Investigator - Curriculum Vitae's and 1572 Forms for Twenty-two New Investigators	IND
475	11 Oct 2005	Mozobil	United States	Serial	Serial 0288 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 3102	IND
476	12 Oct 2005	Mozobil	United States	Serial	Serial 0289 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 3102	IND
477	12 Oct 2005	Mozobil	United States	Serial	Serial 0290 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and CUP001 - Follow-up to Protocol EU21	IND
478	18 Oct 2005	Mozobil	United States	Serial	Serial 0291 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and 2102 - Follow-up to Protocol EU21	IND
479	19 Oct 2005	Mozobil	United States	Serial	Serial 0292 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol CUP001	IND
480	20 Oct 2005	Mozobil	United States	Serial	Serial 0293 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102	IND

481	20 Oct 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. COMMENTS RE: SERIAL #0286 FROM FDA. CONFIRMATION OF NEW CDER ADDRESS. DISCUSSION ABOUT IND SUBMISSION ELECTRONICALLY, AND PEDIATRIC MEETING REQUEST	IND
482	24 Oct 2005	Mozobil	United States	Serial	Serial 0294 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocols 2109 and Corrected Initial Report to Protocol 3102	IND
483	25 Oct 2005	Mozobil	United States	Serial	Serial 0295 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102 and Follow-up to Protocol 3101	IND
484	25 Oct 2005	Mozobil	United States	Serial	Serial 0296 of Mozobil IND 55,851 - Other - Request for Telecon for Protocol 3100 Pediatric Studies	IND
485	25 Oct 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. COPY OF SERIAL #0296 TO DISCUSS PEDIATRIC DEVELOPMENT PROGRAM WAS SENT TO ANN STATEN	IND
486	26 Oct 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. SUMMARY STATEMENT OF 3102 ORPHAN GRANT APPLICATION - FOR ATTENTION OF GARY CALANDRA. GIVEN APPLICATION # 1 R01 FD003104-01	ODD
487	27 Oct 2005	Mozobil	United States	Serial	Serial 0297 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102 and Follow-up to Protocol 2103	IND
488	28 Oct 2005	Mozobil	United States	Serial	Serial 0298 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol CUP001.	IND
489	01 Nov 2005	Mozobil	United States	Serial	Serial 0299 of Mozobil IND 55,851 - Safety Report - Initial to Protocol EU21 - Follow-up to Protocol CUP001	IND
490	03 Nov 2005	Mozobil	United States	Serial	Serial 0300 for Mozobil IND 55,851 - Other - Revised Investigator's Brochure for AMD3100	IND
491	09 Nov 2005	Mozobil	United States	Serial	Serial 0301 to Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101and 3102 - Follow-up to Protocols 2103 and 3101	IND
492	10 Nov 2005	Mozobil	United States	Serial	Serial 0302 to Mozobil IND 55,851 - Safety Report - Initial to Protocol C201	IND
493	14 Nov 2005	Mozobil	United States	Serial	Serial 0303 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101, C201 and CUP - Follow-up to Protocols EU21 and CUP	IND
494	15 Nov 2005	Mozobil	United States	Serial	Serial 0304 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol CUP001	IND
495	16 Nov 2005	Mozobil	United States	Serial	Serial 0305 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2102	IND
496	18 Nov 2005	Mozobil	United States	Serial	Serial 0306 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocols 3102	IND
497	21 Nov 2005	Mozobil	United States	Serial	Serial 0307 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 3102	IND
498	23 Nov 2005	Mozobil	United States	Serial	Serial 0308 of Mozobil IND 55,851 - Safety Report - Corrected Follow-up to Protocol 2103 and Follow-up to CUP001	IND

499	24 Nov 2005	Mozobil	United States	Serial	Serial 0309 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 3101	IND
500	28 Nov 2005	Mozobil	United States	Serial	Serial 0310 of Mozobil IND 55,851 - Safety Report - Initial and follow-up to Protocol 3101	IND
501	30 Nov 2005	Mozobil	United States	Serial	Serial 0311 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol EU21	IND
502	30 Nov 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.ANN STATEN REQUESTED A COPY OF QUESTIONS FROM MEETING PACKAGE, FOR THE PEDIATRICS TELECON IN WORD FORMAT	IND
503	02 Dec 2005	Mozobil	United States	Serial	Serial 0312 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102	IND
504	05 Dec 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil.	IND
505	06 Dec 2005	Mozobil	United States	Serial	Serial 0313 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and CUP001 - Follow-up to Protocol 3102	IND
506	07 Dec 2005	Mozobil	United States	Serial	Serial 0314 of Mozobil IND 55,851 - Safety Report - Follow-up Report to Protocol CUP001	IND
507	08 Dec 2005	Mozobil	United States	Serial	Serial 0315 of Mozobil IND 55,851 - Safety Report - Follow-up Report to Protocol 3102	IND
508	12 Dec 2005	Mozobil	United States	Serial	Serial 0316 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 3101	IND
509	13 Dec 2005	Mozobil	United States	Serial	Serial 0317 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 2112, 3102and CUP001 - Follow-up to Protocol 2109	IND
510	14 Dec 2005	Mozobil	United States	Serial	Serial 0318 of Mozobil IND 55,851 - Safety Report - Initial to Protocols EU21 and 3101 - Follow-up to Protocols EU21 and 3102	IND
511	14 Dec 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FROM WENDY LEE, SECURE EMAIL ADMINISTRATOR, WITH NEW INSTRUCTIONS FOR NEW DOMAIN NAME CHANGE FOR FDA SECURE MESSAGES.	IND
512	16 Dec 2005	Mozobil	United States	Serial	Serial 0319 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and CUP001	IND
513	16 Dec 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. REGARDING PEDIATRIC TELECON TO BE HELD ON DECEMBER 21.	IND
514	19 Dec 2005	Mozobil	United States	Serial	Serial 0320 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101 - Follow-up to Protocols EU21 and CUP	IND

515	20 Dec 2005	Mozobil	United States	Serial	Serial 0321 to Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101	IND
516	20 Dec 2005	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. CONFIRMING THAT WE STILL WANT TO GO AHEAD WITH TELECON ON WEDNESDAY DECEMBER 21 TO DISCUSS PEDIATRIC DEVELOPMENT OF 3100. LIST OF AOM ATTENDEES AND DIAL IN CODE.	IND
517	20 Dec 2005	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. SAE REPORTING DURING CHRISTMAS BREAK AT ANORMED - CONFIRMING THAT FDA WILL ACCEPT FAXES OR EMAILS OF MEDWATCH REPORTS (7 DAY)	IND
518	22 Dec 2005	Mozobil	United States	Serial	Serial 0322 to Mozobil IND 55,851 - Safety Report - Initial to Protocols 2109 and 3102 - Follow-up to Protocol EU21	IND
519	23 Dec 2005	Mozobil	United States	Serial	Serial 0323 of Mozobil IND 55,851 - Safety Report - Initial 3102 and CUP - Follow-up 3102	IND
520	03 Jan 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. ANN STATEN SENT COPY OF PEDIATRIC TELECON MINUTES FROM DECEMBER 21/05 MEETING.	IND
521	04 Jan 2006	Mozobil	United States	Serial	Serial 0324 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001 - Follow-up to Protocol 3102	IND
522	10 Jan 2006	Mozobil	United States	Serial	Serial 0325 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001	IND
523	12 Jan 2006	Mozobil	United States	Serial	Serial 0326 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001	IND
524	13 Jan 2006	Mozobil	United States	Serial	Serial 0327 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101.	IND
525	17 Jan 2006	Mozobil	United States	Serial	Serial 0328 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102.	IND
526	19 Jan 2006	Mozobil	United States	Serial	Serial 0329 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101; Follow-up to Protocol 3102.	IND
527	24 Jan 2006	Mozobil	United States	Serial	Serial 0330 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and 3101	IND
528	25 Jan 2006	Mozobil	United States	Serial	Serial 0331 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101, 3102 and EU21 - Follow-up to Protocol EU21.	IND
529	26 Jan 2006	Mozobil	United States	Serial	Serial 0332 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol AMD3100-EU21	IND
530	27 Jan 2006	Mozobil	United States	Serial	Serial 0333 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102 - Follow-up to Protocol 2109.	IND
531	27 Jan 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. DISCUSSION ON TIMELINES FOR REVISED PEDIATRICS PROTOCOL.	IND

532	30 Jan 2006	Mozobil	United States	Serial	Serial 0334 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102 - Follow-up to Protocol 3101.	IND
533	30 Jan 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. ATTEMPT WAS MADE TO SEND ANN A COPY OF SERIAL NO. 334,	IND
534	31 Jan 2006	Mozobil	United States	Serial	Serial 0335 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 3102	IND
535	01 Feb 2006	Mozobil	United States	Serial	Serial 0336 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102	IND
536	02 Feb 2006	Mozobil	United States	Serial	Serial 0337 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 2105.	IND
537	02 Feb 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FROM WENDY LEE, SECURE EMAIL ADMINISTRATOR, TO CONFIRM PROPER SET-UP.	IND
538	03 Feb 2006	Mozobil	United States	Serial	Serial 0338 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 3102	IND
539	06 Feb 2006	Mozobil	United States	Serial	Serial 0339 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol CUP001	IND
540	07 Feb 2006	Mozobil	United States	Serial	Serial 0340 of Mozobil IND 55,851 - Safety Report - Initial to Protocols CUP001 and 3102.	IND
541	08 Feb 2006	Mozobil	United States	Serial	Serial 0341 of Mozobil IND 55,851 - Safety Report - Follow-up Reports to Protocols 2103, 2112 and 3102.	IND
542	09 Feb 2006	Mozobil	United States	Serial	Serial 0342 of Mozobil IND 55,851 - Safety Report - Initial Reports to Protocols 3101 and 3102 - Follow-up to Protocol 3102.	IND
543	10 Feb 2006	Mozobil	United States	Serial	Serial 0343 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 2102.	IND
544	13 Feb 2006	Mozobil	United States	Serial	Serial 0344 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol AMD3100-CUP001	IND
545	14 Feb 2006	Mozobil	United States	Serial	Serial 0345 of Mozobil IND 55,851 - Safety Report - Initial Report AMD3100-3102 Patient	IND
546	15 Feb 2006	Mozobil	United States	Serial	Serial 0346 of Mozobil IND 55,851 - Safety Report - Initial Report for Protocol AMD3100-3102 - Follow-up Report for Protocols 3101 and 3102.	IND
547	16 Feb 2006	Mozobil	United States	Serial	Serial 0347 of Mozobil IND 55,851 - Safety Report - Initial and Follow-up Reports for Protocol 3101.	IND
548	20 Feb 2006	Mozobil	United States	Serial	Serial 0348 of Mozobil IND 55,851 - Safety Report - Initial and Follow-up Reports for Protocol 3102.	IND
549	22 Feb 2006	Mozobil	United States	Serial	Serial 0349 of Mozobil IND 55,851 - Safety Report - Initial Reports for Protocols 3101 and 3102 - Follow-up Reports for Protocols CUP001, 2103 and 3101.	IND
550	23 Feb 2006	Mozobil	United States	Serial	Serial 0350 for Mozobil IND 55,851 - Safety Reports - Initial to 3101 Protocol	IND
551	23 Feb 2006	Mozobil	United States	Serial	Serial 0351 to Mozobil IND 55,851 - Other - Cross Reference Authorization -	IND

552	24 Feb 2006	Mozobil	United States	Serial	Serial 0352 to Mozobil IND 55,851 - Safety Report - Initial to Protocols 2109 and 3102	IND
553	27 Feb 2006	Mozobil	United States	Serial	Serial 0353 of Mozobil IND 55,851 - Safety Report - Initial and Follow-up to Protocol 3102.	IND
554	28 Feb 2006	Mozobil	United States	Serial	Serial 0354 of Mozobil IND 55,851 - Safety Report - Initial 3101 and 3102 - Follow-up 3102	IND
555	01 Mar 2006	Mozobil	United States	Serial	Serial 0355 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 3102	IND
556	03 Mar 2006	Mozobil	United States	Serial	Serial 0356 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102 - Follow-up to Protocol CUP001	IND
557	07 Mar 2006	Mozobil	United States	Serial	Serial 0357 of Mozobil IND 55,851 - Safety Report - Initial EU21 and CUP - Follow-up EU21	IND
558	07 Mar 2006	Mozobil	United States	Serial	Serial 0358 of Mozobil IND 55,851 - Safety Report -	IND
559	08 Mar 2006	Mozobil	United States	Serial	Serial 0359 of Mozobil IND 55,851 - Other - Request for Single Patient Exception - Patient	IND
560	08 Mar 2006	Mozobil	United States	Serial	Serial 0360 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and 3101	IND
561	08 Mar 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. A COPY OF SERIAL NO. 0359 WAS SENT TO ANN STATEN TO REQUEST SINGLE PATIENT EXCEPTION.	IND
562	09 Mar 2006	Mozobil	United States	Serial	Serial 0361 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101 - Follow-up to Protocols 3101 and 3102	IND
563	09 Mar 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. A NEW FAX NUMBER FOR ANN STATEN, REGULATORY PROJECT MANAGER IS REPORTED	IND
564	13 Mar 2006	Mozobil	United States	Serial	Serial 0362 of Mozobil IND 55,851 - General Correspondence and Protocol Amendment - New Investigator - - Six New Investigators	IND
565	14 Mar 2006	Mozobil	United States	Serial	Serial 0363 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001 - Follow-up to Protocols 2103 and CUP001	IND
566	15 Mar 2006	Mozobil	United States	Serial	Serial 0364 of Mozobil IND 55,851 - Safety Report - Initial and Follow-up to Protocol C201	IND
567	17 Mar 2006	Mozobil	United States	Serial	Serial 0365 of Mozobil IND 55,851 - Safety Report - Initial to Protocol C201 - Follow-up to Protocol 2103	IND
568	20 Mar 2006	Mozobil	United States	Serial	Serial 0366 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and CUP001	IND
569	22 Mar 2006	Mozobil	United States	Serial	Serial 0367 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102 - Follow-up to Protocols 2112 and CUP001.	IND

570	24 Mar 2006	Mozobil	United States	Serial	Serial 0368 of Mozobil IND 55,851 - Safety Report - Initial 3102 and CUP001 - Follow-up C201 and 3102	IND
571	27 Mar 2006	Mozobil	United States	Serial	Serial 0369 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and 2112 - Follow-up to Protocol 2103	IND
572	28 Mar 2006	Mozobil	United States	Serial	Serial 0370 for Mozobil IND 55,851 - Safety Reports - Initial to Protocols EU21 and CUP001	IND
573	29 Mar 2006	Mozobil	United States	Serial	Serial 0371 to Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and CUP001	IND
574	30 Mar 2006	Mozobil	United States	Serial	Serial 0372 to Mozobil IND 55,851 - Information Amendment - Pharmacology-Toxicology - Summaries and Final Reports for Two Studies -	IND
575	30 Mar 2006	Mozobil	United States	Serial	Serial 0373 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 2108	IND
576	31 Mar 2006	Mozobil	United States	Serial	Serial 0374 of Mozobil IND 55,851 - Safety Report - Initial EU21 and 3102	IND
577	31 Mar 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
578	03 Apr 2006	Mozobil	United States	Serial	Serial 0375 of Mozobil IND 55,851 - Safety Report - Initial to Protocols EU21 and CUP001 - Follow-up to Protocol EU21	IND
579	04 Apr 2006	Mozobil	United States	Serial	Serial 0376 of Mozobil IND 55,851 - Safety Report - Initial to Protocols CUP001 and 3102 - Follow-up to Protocol 3102	IND
580	06 Apr 2006	Mozobil	United States	Serial	Serial 0377 of Mozobil IND 55,851 - Safety Report - Follow-up 3102	IND
581	08 Apr 2006	Mozobil	United States	Serial	Serial 0378 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and C201	IND
582	10 Apr 2006	Mozobil	United States	Serial	Serial 0379 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102 - Follow-up to Protocols 3101 and 3102	IND
583	10 Apr 2006	Mozobil	United States	Serial	Serial 0380 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101 - Follow-up to Protocols C201, 3102 and CUP001	IND
584	10 Apr 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. PROTOCOLS 3101 AND 3102 WERE SENT TO ANN STATEN, AS PER HER REQUEST	IND
585	11 Apr 2006	Mozobil	United States	Serial	Serial 0381 of Mozobil IND 55,851 - General Correspondence - Progress on Pediatrics	IND
586	13 Apr 2006	Mozobil	United States	Serial	Serial 0382 of Mozobil IND 55,851 - Protocol Amendment - Changes to Protocol AMD3100-2112	IND
587	13 Apr 2006	Mozobil	United States	Serial	Serial 0383 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102 - Follow-up to Protocols 3102, EU21, 2104 and 3101	IND
588	19 Apr 2006	Mozobil	United States	Serial	Serial 0384 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102	IND
589	21 Apr 2006	Mozobil	United States	Serial	Serial 0385 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102 - Follow-up to Protocol 3102	IND
590	24 Apr 2006	Mozobil	United States	Serial	Serial 0386 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102	IND

591	25 Apr 2006	Mozobil	United States	Serial	Serial 0387 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101.	IND
592	26 Apr 2006	Mozobil	United States	Serial	Serial 0388 of Mozobil IND 55,851 - Safety Report - Initial Report to Protocol 2108	IND
593	26 Apr 2006	Mozobil	United States	Serial	Serial 0389 of Mozobil IND 55,851 - Protocol Amendment - New Protocols 3101-LTF and 3102-LTF	IND
594	27 Apr 2006	Mozobil	United States	Serial	Serial 0390 for Mozobil IND 55,851 - Safety Reports - Initial to CUP001 Protocol - Follow-up to 3101 Protocol	IND
595	27 Apr 2006	Mozobil	United States	Contact Report	Bem Atsma cntacted Lt. Karl Stiller at FDA	IND
596	02 May 2006	Mozobil	United States	Serial	Serial 0391 to Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101 - Follow-up to Protocols 2104 and 3102	IND
597	03 May 2006	Mozobil	United States	Serial	Serial 0392 to Mozobil IND 55,851 - Safety Report - Follow-up to Protocols EU21 and 2112 and 3102 and CUP001	IND
598	04 May 2006	Mozobil	United States	Serial	Serial 0393 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102 - Follow-up to Protocol EU21	IND
599	05 May 2006	Mozobil	United States	Serial	Serial 0394 of Mozobil IND 55,851 - Protocol Amendment, New Investigators - Twenty-one New Investigators	IND
600	08 May 2006	Mozobil	United States	Serial	Serial 0395 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101 - Follow-up to Protocols 3101 and 3102	IND
601	09 May 2006	Mozobil	United States	Serial	Serial 0396 of Mozobil IND 55,851 - Safety Report - Initial to Protocol CUP001 - Follow-up to Protocols 3101 and 3102	IND
602	10 May 2006	Mozobil	United States	Serial	Serial 0397 of Mozobil IND 55,851 - Protocol Amendment, Change in Protocol - CUP001	IND
603	10 May 2006	Mozobil	United States	Serial	Serial 0398 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102 - Follow-up to Protocols 3101 and CUP001	IND
604	11 May 2006	Mozobil	United States	Serial	Serial 0399 of Mozobil IND 55,851 - Safety Report - Initial to Protocol C201 - Follow-up to Protocols 3101 and 3102	IND
605	12 May 2006	Mozobil	United States	Serial	Serial 0400 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3102 and CUP001	IND
606	15 May 2006	Mozobil	United States	Serial	Serial 0401 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocol 3102	IND
607	16 May 2006	Mozobil	United States	Serial	Serial 0402 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101	IND
608	17 May 2006	Mozobil	United States	Serial	Serial 0403 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3101 - Follow-up to Protocol 3101	IND
609	18 May 2006	Mozobil	United States	Serial	Serial 0404 of Mozobil IND 55,851 - Safety Report - Follow-up to Protocols 2103 and 2104	IND
610	19 May 2006	Mozobil	United States	Serial	Serial 0405 of Mozobil IND 55,851 - Safety Report - Initial to Protocols 3101 and 3102-CA and CUP001 - Follow-up to Protocols 2104 and EU21	IND
611	23 May 2006	Mozobil	United States	Serial	Serial 0406 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102	IND
612	24 May 2006	Mozobil	United States	Serial	Serial 0407 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102 - Follow-up to Protocol EU21	IND

613	25 May 2006	Mozobil	United States	Serial	Serial 0408 of Mozobil IND 55,851 - General Correspondence -	IND
614	25 May 2006	Mozobil	United States	Serial	Serial 0409 of Mozobil IND 55,851 - Safety Report - Initial to Protocol 3102	IND
615	29 May 2006	Mozobil	United States	Serial	Serial 0410 for Mozobil IND 55,851 - Safety Reports Regarding Protocols 2104, 3101 and 3102.	IND
616	30 May 2006	Mozobil	United States	Serial	Serial 0411 for Mozobil IND 55,851 - Safety Reports Regarding Protocol 3102, Involving Patient	IND
617	31 May 2006	Mozobil	United States	Serial	Serial 0412 for Mozobil IND 55,851 - Safety Reports Regarding Protocol EU21, Involving Patient	IND
618	02 Jun 2006	Mozobil	United States	Serial	Serial 0413 for Mozobil IND 55,851 - Safety Reports Regarding Protocols 2104, 2105, 3101 and 3102.	IND
619	02 Jun 2006	Mozobil	United States	Serial	Serial 0414 for Mozobil IND 55,851 - Safety Reports Regarding Protocols EU21, CUP001 , and 3101.	IND
620	06 Jun 2006	Mozobil	United States	Serial	Serial 0415 for Mozobil IND 55,851 - Safety Reports Regarding Protocols CUP001 and 2102, Involving Patients	IND
621	09 Jun 2006	Mozobil	United States	Serial	Serial 0416 for Mozobil IND 55,851 - Safety Reports Regarding Protocols CUP001, 3101 and 3102.	IND
622	09 Jun 2006	Mozobil	United States	Serial	Serial 0417 - for Mozobil IND 55,851 General Correspondence - Request for CMC Teleconference for Type C Meeting.	IND
623	09 Jun 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. COPY OF SERIAL 0417 SENT TO ANN STATEN TO BEGIN PLANNING TELECON.	IND
624	09 Jun 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. LETTER SENT TO FOI, TO REQUEST COPY OF INFORMATION REGARDING STEMGEN AND NEUPOGEN. CONFIRMATION LETTERS FROM FDA WERE RECEIVED ON JUNE 09 WITH REFERENCE NUMBERS 2006-9381 AND 2006-9382	IND
625	12 Jun 2006	Mozobil	United States	Serial	Serial 0418 for Mozobil IND 55,851 - Safety Report Regarding Follow-up to Protocol EU21 Involving Patient -	IND
626	12 Jun 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
627	13 Jun 2006	Mozobil	United States	Serial	Serial 0419 for Mozobil IND 55,851 - Safety Reports Regarding Follow-up to Protocol 3102 Involving Patients	IND
628	13 Jun 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. CMC TELECON REQUEST SENT TO ANN STATEN.	IND

629	14 Jun 2006	Mozobil	United States	Serial	Serial 0420 for Mozobil IND 55,851 - Safety Reports - Initial Reports Regarding Protocols CUP001and 3101,Involving Patients	IND
630	15 Jun 2006	Mozobil	United States	Serial	Serial 0421 for Mozobil IND 55,851 - Safety Reports - Regarding Protocols 2108 and 3102, Involving Patients	IND
631	16 Jun 2006	Mozobil	United States	Serial	Serial 0422 for Mozobil IND 55,851 - Safety Report - Initial Report Regarding Protocol 3101, Involving Patient	IND
632	19 Jun 2006	Mozobil	United States	Serial	Serial 0423 for Mozobil IND 55,851 - Safety Reports - Regarding Protocols 3101 and 3102, Involving Patient	IND
633	20 Jun 2006	Mozobil	United States	Serial	Serial 0424 for Mozobil IND 55,851 - Safety Report - Initial Reports Regarding Protocols 3101, 3102 and CUP001, Involving Patients	IND
634	20 Jun 2006	Mozobil	United States	Contact Report	Bern Atsma called Lt Karl Stiller to check on the progress for the CMC teleconference preparations	IND
635	21 Jun 2006	Mozobil	United States	Serial	Serial 0425 for Mozobil IND 55,851 - Safety Report - Initial Reports Regarding Protocols 3101 and 3102, Involving Patients	IND
636	21 Jun 2006	Mozobil	United States	Contact Report	Lt Karl Stiller left a voicemail for Gary Bridger (US Agent) stating the proposed time for the CMC teleconference would be 25 July 2006 at 9 - 10 AM EDT	IND
637	23 Jun 2006	Mozobil	United States	Serial	Serial 0426 for Mozobil IND 55,851 - Safety Report - Regarding Protocols 3101 and 3102, Involving Patients	IND
638	26 Jun 2006	Mozobil	United States	Serial	Serial 0427 for Mozobil IND 55,851 - Safety Reports - Regarding Protocols 3101 and 3102, Involving Patients	IND
639	27 Jun 2006	Mozobil	United States	Serial	Serial 0428 for Mozobil IND 55,851 - Safety Reports - Initial and Follow-up Regarding Protocol 3102, Involving Patients	IND
640	27 Jun 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. PDF COPY ATTACHED OF THE CMC INFORMATION PACKAGE (SERIAL #0429) SENT TO KARL STILLER, IN PREPARATION OF TELECON SCHEDULED 25 JULY 2006.	IND
641	28 Jun 2006	Mozobil	United States	Serial	Serial 0430 for Mozobil IND 55,851 - Safety Reports Regarding Protocols CUP001, 3101 and 3102.	IND
642	28 Jun 2006	Mozobil	United States	Serial	Serial 0429 - CMC Teleconference Information Package for Type C Meeting	IND
643	29 Jun 2006	Mozobil	United States	Serial	Serial 0431 for Mozobil IND 55,851 - Safety Reports Involving Protocols 3101 and 3102.	IND
644	30 Jun 2006	Mozobil	United States	Serial	Serial 0432 for Mozobil IND 55,851 - Safety Reports Regarding Protocols 3101 and 3102.	IND
645	04 Jul 2006	Mozobil	United States	Serial	Serial 0433 for Mozobil IND 55,851 - Safety Report Regarding Protocol 3102, Involving Patient	IND
646	05 Jul 2006	Mozobil	United States	Serial	Serial 0434 for Mozobil IND 55,851 - Annual Report to Cover Reporting Period From May 6, 2005 to May 5, 2006.	IND

647	05 Jul 2006	Mozobil	United States	Serial	Serial 0435 for Mozobil IND 55,851 - Safety Reports Regarding Protocols CUP001 and 3102. Involving Patients	IND
648	06 Jul 2006	Mozobil	United States	Serial	Serial 0436 for Mozobil IND 55,851 - Safety Report Regarding Protocol 3101, Involving Patient	IND
649	07 Jul 2006	Mozobil	United States	Serial	Serial 0437 for Mozobil IND 55,851 - Safety Reports Regarding Protocols CUP001 and 3102.	IND
650	10 Jul 2006	Mozobil	United States	Serial	Serial 0438 for Mozobil IND 55,851 - Safety Reports Regarding Protocol 3101, Involving Patients	IND
651	11 Jul 2006	Mozobil	United States	Serial	Serial 0439 for Mozobil IND 55,851 - Safety Reports Regarding Protocol CUP001, Involving Patients	IND
652	11 Jul 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. STATISTICAL COMMENTS REGARDING THE LONG TERM FOLLOW-UP PROTOCOLS FROM THE AGENCY	IND
653	11 Jul 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. CONFIRMATION LETTER RECEIVED BY GARY BRIDGER (DATED 21 JUNE 2006) FOR DATE AND TIME OF CMC TELECON SCHEDULED FOR 25 JULY 2006, WITH LIST OF CDER ATTENDEES	IND
654	12 Jul 2006	Mozobil	United States	Serial	Serial 0440 for Mozobil IND 55,851 - Safety Reports Regarding Protocols 3101 and 3102, Involving Patients	IND
655	12 Jul 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA	IND
656	13 Jul 2006	Mozobil	United States	Serial	Serial 0441 for Mozobil IND 55,851 - Protocol Amendment, New Investigators for Protocols 3102 (4), 3101 (3) and CUP001 (38).	IND
657	13 Jul 2006	Mozobil	United States	Serial	Serial 0442 for Mozobil IND 55,851 - General Correspondence, Response to FDA Comments Regarding Phase 3 Statistical Analysis Plan.	IND
658	14 Jul 2006	Mozobil	United States	Serial	Serial 0443 for Mozobil IND 55,851 - Safety Reports Regarding Protocols 3102 and CUP001	IND
659	14 Jul 2006	Mozobil	United States	Serial	Serial 0444 for Mozobil IND 55,851 - Safety Reports Regarding Protocols CUP001 and 3102, Involving Patients	IND
660	19 Jul 2006	Mozobil	United States	Serial	Serial 0445 for Mozobil IND 55,851 - Safety Reports Regarding Protocols CUP001, 3101 and 3102.	IND
661	24 Jul 2006	Mozobil	United States	Serial	Serial 0446 for Mozobil IND 55,851 - Safety Reports Regarding Protocols 3101 and 3102.	IND
662	25 Jul 2006	Mozobil	United States	Serial	Serial 0447 for Mozobil IND 55,851 - Safety Reports Regarding Protocols SPU001, 3102 and 3101.	IND

663	26 Jul 2006	Mozobil	United States	Serial	Serial 0448 for Mozobil IND 55,851 - Pharm/Tox Amendment - Preclinical Study Reports and References Submitted to FDA.	IND
664	26 Jul 2006	Mozobil	United States	Serial	Serial 0449 for Mozobil IND 55,851 - Safety Reports Regarding Protocols CUP001 and 3102, Involving Patients	IND
665	27 Jul 2006	Mozobil	United States	Serial	Serial 0450 for Mozobil IND 55,851 - Safety Reports Regarding CUP001 Protocol.	IND
666	28 Jul 2006	Mozobil	United States	Serial	Serial 0451 for Mozobil IND 55,851 - Initial and Follow-up Safety Reports Regarding Protocols 3101, 3102 and C201.	IND
667	31 Jul 2006	Mozobil	United States	Serial	Serial 0452 for Mozobil IND 55,851 - Initial Safety Report Regarding Protocol 3101.	IND
668	01 Aug 2006	Mozobil	United States	Serial	Serial 0453 for Mozobil IND 55,851 - Initial and Follow-up Safety Reports Regarding Protocols CUP001, 3101 and 3102.	IND
669	03 Aug 2006	Mozobil	United States	Serial	Serial 0454 for Mozobil IND 55,851 - Initial and Follow-up Safety Reports Regarding Protocols CUP001 and 3102.	IND
670	04 Aug 2006	Mozobil	United States	Serial	Serial 0455 for Mozobil IND 55,851 - Initial and Follow-up Safety Reports Regarding Protocol 3102.	IND
671	08 Aug 2006	Mozobil	United States	Serial	Serial 0456 for Mozobil IND 55,851 - Initial and Follow-up Safety Reports Regarding Protocols 3102, EU21 and CUP001.	IND
672	09 Aug 2006	Mozobil	United States	Serial	Serial 0457 for Mozobil IND 55,851 - Request for Single Patient Exception Using Protocol CUP001.	IND
673	09 Aug 2006	Mozobil	United States	Serial	Serial 0458 for Mozobil IND 55,851 - Initial and Follow-up Safety Reports Regarding Protocols 3101, 3102 and CUP001.	IND
674	09 Aug 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. Official FDA Meeting Minutes From CMC Type B Meeting Held on 25 July 2006	IND
675	09 Aug 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. A COPY OF SERIAL #0457 WAS SENT TO DOTTI PEASE REQUESTING EXCEPTION FOR SINGLE PATIENT USE FOR PATIENT	IND
676	10 Aug 2006	Mozobil	United States	Serial	Serial 0459 for Mozobil IND 55,851 - Safety Reports - Initial Report for Protocol 3102 and a Follow-up Report for CUP001.	IND
677	10 Aug 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. APPROVAL FROM DOTTI PEASE TO TREAT PATIENT RE: SERIAL #0457.	IND
678	11 Aug 2006	Mozobil	United States	Serial	Serial 0460 for Mozobil IND 55,851 - Safety Report - Follow-up Report Regarding CUP001 Protocol for Patient	IND
679	14 Aug 2006	Mozobil	United States	Serial	Serial 0461 for Mozobil IND 55,851 - Safety Report - Initial for Protocol 3102, Regarding Patients	IND
680	15 Aug 2006	Mozobil	United States	Serial	Serial 0462 for Mozobil IND 55,851 - Safety Reports - Initial for Protocols 3102 and CUP, Regarding Patients	IND
681	16 Aug 2006	Mozobil	United States	Serial	Serial 0463 for Mozobil IND 55,851 - Safety Reports - Initial and Follow-up for Protocols 3102 and CUP Involving 12 Patients.	IND

682	18 Aug 2006	Mozobil	United States	Serial	Serial 0464 for Mozobil IND 55,851 - Safety Report - Initial Reports for Protocols 3101 and 3102, Regarding Patients	IND
683	18 Aug 2006	Mozobil	United States	Serial	Serial 0465 for Mozobil IND 55,851 - Safety Report - Initial and Follow-up for Protocols 3101 and CUP001.	IND
684	22 Aug 2006	Mozobil	United States	Serial	Serial 0466 for Mozobil IND 55,851 - Safety Report - Initial Reports Regarding Protocols 3101 and 3102 and CUP001 - Follow-up Reports Regarding Protocols 3101 and 3102.	IND
685	24 Aug 2006	Mozobil	United States	Serial	Serial 0467 for Mozobil IND 55,851 - Safety Report - Initial Reports Regarding Protocols 3101 and CUP001 - Follow-up Reports Regarding Protocols 3102 and CUP001.	IND
686	25 Aug 2006	Mozobil	United States	Serial	Serial 0468 for Mozobil IND 55,851 - Safety Report - Initial Report Regarding Protocol 3101 Involving Patient	IND
687	29 Aug 2006	Mozobil	United States	Serial	Serial 0469 for Mozobil IND 55,851 - Safety Report - Follow-up Report Regarding Protocol 3102 Involving Patient	IND
688	30 Aug 2006	Mozobil	United States	Serial	Serial 0470 for Mozobil IND 55,851 - Safety Report - Initial 2103 and 3102 - Follow-up 3102 and CUP001	IND
689	31 Aug 2006	Mozobil	United States	Serial	Serial 0471 for Mozobil IND 55,851 - Protocol Amendment, New Investigator - Twenty-two New Investigators.	IND
690	31 Aug 2006	Mozobil	United States	Serial	Serial 0472 for Mozobil IND 55,851 - Safety Report - Initial and Follow-up for Protocol 3101 and CUP001.	IND
691	31 Aug 2006	Mozobil	United States	Serial	Serial 0473 for Mozobil IND 55,851 - Other - Request for Single Patient Exception - Patient Using Protocol CUP001	IND
692	31 Aug 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. regarding CSRs and CRFs prior to Pre-NDA meeting	IND
693	31 Aug 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil.	IND
694	31 Aug 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. A COPY OF SERIAL #0473 WAS SENT TO DOTTI PEASE REQUESTING EXCEPTION FOR SINGLE PATIENT USE	IND
695	01 Sep 2006	Mozobil	United States	Serial	Serial 0474 for Mozobil IND 55,851 - Protocol Amendment, New Protocol - AMD3100-2201.	IND
696	06 Sep 2006	Mozobil	United States	Serial	Serial 0475 for Mozobil IND 55,851 - Safety Report - Follow-up Reports to 3102 and CUP001.	IND
697	07 Sep 2006	Mozobil	United States	Serial	Serial 0476 for Mozobil IND 55,851 - Safety Report - Initial and Follow-up Reports for 3102 and CUP001.	IND
698	12 Sep 2006	Mozobil	United States	Serial	Serial 0477 for Mozobil IND 55,851 - Safety Report - Initial and Follow-up for 3101, 3102 and CUP001.	IND
699	14 Sep 2006	Mozobil	United States	Serial	Serial 0478 for Mozobil IND 55,851, - Protocol Amendment Change in Protocol - Amendment 1 to Protocol 2112.	IND

700	18 Sep 2006	Mozobil	United States	Serial	Serial 0479 for Mozobil IND 55,851 - Safety Report - Initial and Follow-up for 3101, 3102 and CUP001.	IND
701	18 Sep 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FOLLOW-UP TO EMAIL ON AUGUST 31.	IND
702	20 Sep 2006	Mozobil	United States	Annual Report	Annual Report for Mozobil ODD 03-1679 covering the reporting period 10 Sep 2005 through 10 Sep 2006.	ODD
703	21 Sep 2006	Mozobil	United States	Serial	Serial 0480 for Mozobil IND 55,851 - Safety Report - Initial and Follow-up for 3101, 3102 and CUP001.	IND
704	25 Sep 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. RESPONSE RECEIVED FROM DOTTI PEASE	IND
705	03 Oct 2006	Mozobil	United States	Serial	Serial 0481 for Mozobil IND 55,851 - Protocol Amendment, New Investigator - Ten New Investigators involved in Protocol CUP001.	IND
706	09 Nov 2006	Mozobil	United States	Serial	Serial 0482 for Mozobil IND 55,851 - Information Amendment, Clinical - Compassionate Use Program Interim Report.	IND
707	15 Nov 2006	Mozobil	United States	Serial	Serial 0483 for Mozobil IND 55,851 - Other - Request for Single Patient Exception - Patient	IND
708	15 Nov 2006	Mozobil	United States	Serial	Serial 0484 for Mozobil IND 55,851 - Protocol Amendment, New Investigator - Five New Investigators Regarding Protocol CUP001.	IND
709	15 Nov 2006	Mozobil	United States	Serial	Serial 0485 for Mozobil IND 55,851 - Safety Report - Initial 3101	IND
710	20 Nov 2006	Mozobil	United States	Correspondence Sent	Correspondence sent regarding IND 55, 851 for Mozobil. DISCUSSIONS REGARDING APPROVAL OF CUP PATIENT	IND
711	28 Nov 2006	Mozobil	United States	Serial	Serial 0486 for Mozobil IND 55,851 - Other - Revised Investigator Brochure, Version 11.	IND
712	06 Dec 2006	Mozobil	United States	Serial	Serial 0487 for Mozobil IND 55,851 - General Correspondence - Transfer of Ownership from AnorMED Inc.to Genzyme Corp.	IND
713	06 Dec 2006	Mozobil	United States	Correspondence Sent	Letter for Transfer of Ownership of ODA 03-1679 to Genzyme.	ODD
714	13 Dec 2006	Mozobil	United States	Serial	Serial 0488 for Mozobil IND 55,851 - General Correspondence - Request for Transfer of Administrative Ownership from AnorMED to Genzyme.	IND
715	13 Dec 2006	Mozobil	United States	Correspondence Sent	Letter to Accept and Confirm Transfer of Ownership of OPD 03-1679 From AnorMED	ODD
716	20 Dec 2006	Mozobil	United States	Serial	Serial 0489 for Mozobil IND 55,851 - Protocol Amendment, New Investigator - 1572s and CV for Principal Investigators for CUP001.	IND

717	20 Dec 2006	Mozobil	United States	Correspondence Received	Correspondence received regarding IND 55, 851 for Mozobil. FDA NOTIFICATION OF CHANGE FROM Anormed TO GENZYME	IND
718	09 Jan 2007	Mozobil	United States	Correspondence Sent	Fax Copy of Serial 0490, Containing a Request for Single Exception Use of AMD3100 (Mozobil) for Patient	IND
719	09 Jan 2007	Mozobil	United States	Serial	Serial 0490 for Mozobil IND 55,851 - Other - Request for Single Patient Exception - Patient	IND
720	10 Jan 2007	Mozobil	United States	Correspondence Received	Email correspondence between Bem Atsma and Dotti Pease at FDA.	IND
721	11 Jan 2007	Mozobil	United States	Correspondence Received	Correspondence received from FDA regarding Mozobil IND 55,851 that acknowledges receipt of the AnorMED notification of their name change to AnorMED Corp. of Genzyme Corp.	IND
722	17 Jan 2007	Mozobil	United States	Serial	Serial 0491, Protocol Amendment New Investigator for IND 55,851 regarding Mozobil.	IND
723	09 Feb 2007	Mozobil	United States	Serial	Serial 0493, Protocol Amendment - Change in Protocol for IND 55,851 Mozobil Protocol AMD3100-2112.	IND
724	09 Feb 2007	Mozobil	United States	Serial	Serial 0492 Cross Reference Authorization for IND 55,851 Mozobil.	IND
725	12 Feb 2007	Mozobil	United States	Correspondence Received	Email from Dotti Pease at CDER	IND
726	15 Feb 2007	Mozobil	United States	Serial	Serial 0494 Initial Safety Report for IND 55,851 Mozobil Patient	IND
727	19 Feb 2007	Mozobil	United States	Serial	Serial 0495 Request for Single Patient Exception for IND 55,851 Mozobil Patient	IND
728	20 Feb 2007	Mozobil	United States	Correspondence Received	Email correspondence between Bem Atsma and Dotti Pease at FDA.	IND
729	23 Feb 2007	Mozobil	United States	Serial	Serial 0496 Follow-up Safety Report for IND 55,851 Mozobil Patient	IND
730	12 Mar 2007	Mozobil	United States	Serial	Serial 0497 Request for Single Patient Exception Regarding Mozobil IND 55,851 as per Protocol CUP001.	IND
731	13 Mar 2007	Mozobil	United States	Correspondence Received	Email Received from Dotti Pease at CDER Giving Approval to Treat Patient Using Mozobil IND 55,851, Under Protocol CUP001.	IND
732	19 Mar 2007	Mozobil	United States	Serial	Serial 0498 Protocol Amendment Regarding Mozobil IND 55,851, New Investigators for Protocol CUP001.	IND
733	21 Mar 2007	Mozobil	United States	Serial	Serial 0499 Protocol Amendment, Change in Protocol for IND 55,851 Regarding Mozobil, Protocol AMD3100-1101 Amendment 3.	IND
734	22 Mar 2007	Mozobil	United States	Serial	Serial 0500 IND 55,851 Request for Comment Regarding Proposal for CUP Data Presentation in Planned Mozobil NDA.	IND
735	27 Mar 2007	Mozobil	United States	Serial	Serial 0501 CMC Type C Meeting Request Regarding Mozobil IND 55,851 for Upcoming NDA.	IND
736	27 Mar 2007	Mozobil	United States	Correspondence Sent	A Copy of Serial 0501 CMC Type C Meeting Request Sent to Dotti Pease at CDER.	IND
737	30 Mar 2007	Mozobil	United States	Correspondence Sent	A Copy of Serial 0502 Was Emailed and Faxed to FDA	IND

738	30 Mar 2007	Mozobil	United States	Serial	Serial 0502 Single Patient Exception Request to use Mozobil IND 55,851 as per Protocol CUP001 fpr Patient	IND
739	02 Apr 2007	Mozobil	United States	Correspondence Sent	Confirmation was Sent to the FDA That 6 June 2007 at 2:00pm is Acceptable for the Requested Mozobil CMC Type C Meeting.	IND
740	03 Apr 2007	Mozobil	United States	Correspondence Received	Letter Received from Scott Goldie at CDER Regarding Confirmation of the CMC Type C Meeting for IND 55,851 Mozobil Scheduled for Wednesday, 6 June 2007 at 14:00 ET.	IND
741	03 Apr 2007	Mozobil	United States	Correspondence Received	Email sent from Dotti Pease at CDER Giving Approval to Treat Compassionate Use Patient With IND 55,851 Mozobil.	IND
742	05 Apr 2007	Mozobil	United States	Correspondence Received	Email Response From Dotti Pease at CDER	IND
743	16 Apr 2007	Mozobil	United States	Serial	Serial 0503, Safety Report for Mozobil IND 55,851 Follow-up Information for Patient Enrolled in Protocol AMD3100-3102	IND
744	07 May 2007	Mozobil	United States	Serial	Serial 0504 - Other - Mozobil IND 55,851 Single Patient Exception Request for Protocol CUP001.	IND
745	07 May 2007	Mozobil	United States	Correspondence Sent	A Copy of Serial 0504 to Mozobil IND 55,851 was Faxed	IND
746	07 May 2007	Mozobil	United States	Correspondence Sent	Email to Scott Goldie Regarding Number of Desk Copies of CMC Type C Meeting to be Sent, and Confirm Address.	IND
747	08 May 2007	Mozobil	United States	Serial	Serial 0505 - Other - Mozobil IND 55,851 CMC Type C Meeting Information Package.	IND
748	11 May 2007	Mozobil	United States	Serial	Serial 0506 for Mozobil IND 55,851 - Safety Report Regarding Protocol CUP001, Involving Patient	IND
749	14 May 2007	Mozobil	United States	Correspondence Sent	A Copy of MedWatch MOZO-10037	IND
750	16 May 2007	Mozobil	United States	Correspondence Received	2007-05-16 - Email from Dotti Pease in Response to a Request to Hold a Telecon to Introduce Key Regulatory Members.	IND
751	17 May 2007	Mozobil	United States	Serial	Serial 0507 for Mozobil IND 55,851 - Safety Report for Protocol AMD3100-CUP001 MOZO-10034.	IND
752	21 May 2007	Mozobil	United States	Serial	Serial 0508 Mozobil IND 55,851 Safety Report - for Protocol AMD3100-CUP001 MOZO-10037 Follow-up	IND
753	25 May 2007	Mozobil	United States	Serial	Serial 0509 - CUP001 Protocol Amendment New Investigators for Mozobil IND 55,851.	IND
754	25 May 2007	Mozobil	United States	Serial	Serial 0510 - Safety Report Follow-up Report MOZO-10034 to Protocol CUP001 Mozobil IND 55,851.	IND
755	04 Jun 2007	Mozobil	United States	Correspondence Received	FDA's Preliminary Responses to our Meeting Package In Preparation for the Type C Meeting to be Held 6 June 2007.	IND
756	06 Jun 2007	Mozobil	United States	Serial	Serial 0511 of Mozobil IND 55,851 - Safety Report, Follow-up Regarding Protocol AMD3100-3101,	IND

757	13 Jun 2007	Mozobil	United States	Serial	Serial 0512 of Mozobil IND 55,851 - Single Patient Exception Request for 14 year old Female,	IND
758	13 Jun 2007	Mozobil	United States	Correspondence Sent	Serial 0512 for Mozobil IND 55,851 was Faxed to FDA to Request Treatment of a 14 Year Old Female Patient.	IND
759	14 Jun 2007	Mozobil	United States	Correspondence Received	Email Received From Dotti Pease at CDER Giving Approval to Treat Patient (See Serial #0512).	IND
760	14 Jun 2007	Mozobil	United States	Correspondence Received	Official FDA Minutes From Mozobil Type C CMC Meeting TeleconfereMce Held on 6 June 2007.	IND
761	22 Jun 2007	Mozobil	United States	Serial	Serial 0513 to Mozobil IND 55,851 - Electronic Dataset Format Confirmation.	IND
762	25 Jun 2007	Mozobil	United States	Serial	Serial 0514 of Mozobil IND 55,851 - Minutes from CMC Type C Meeting Held 6 June 2007.	IND
763	29 Jun 2007	Mozobil	United States	Serial	Serial 0515 for Mozobil IND 55,851 - Annual Report Covering Reporting Period from 6 May 2006 to 5 May 2007	IND
764	18 Jul 2007	Mozobil	United States	Correspondence Sent	Correspondence to Mozobil IND 55,851; Genzyme's press release of the non-Hodgkin's lymphoma phase 3 trial - Protocol AMD3100-3101	IND
765	25 Jul 2007	Mozobil	United States	Serial	Serial 0516 to IND 55,851 for Mozobil; transfer of primary contact for Mozobil	IND
766	27 Jul 2007	Mozobil	United States	Correspondence Received	Correspondence to Mozobil IND 55,851; regarding serial S513,	IND
767	31 Jul 2007	Mozobil	United States	Serial	Serial 0517 to IND 55,851 for Mozobil; 3 IND Safety Report Follow-up 001 reports: AMD3100-3101/MOZO-10128, AMD3100-3101/MOZO-10157, and AMD3100-3101/MOZO-10129	IND
768	01 Aug 2007	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; advance notice of a press release announcing the top line results of protocol AMD3100-3102	IND
769	02 Aug 2007	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; press release announcing the top line results of protocol AMD3100-3102	IND
770	02 Aug 2007	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; response to FDA queries about pre-NDA and NDA timelines	IND
771	03 Aug 2007	Mozobil	United States	Serial	Serial 0518 to IND 55,851 for Mozobil; request for a Type B meeting, a pre-NDA meeting	IND
772	08 Aug 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; discussion and confirmation of pre-NDA meeting date and time	IND
773	10 Aug 2007	Mozobil	United States	Serial	Serial 0519 to IND 55,851 for Mozobil; submission of a new protocol, MOZ00207	IND
774	15 Aug 2007	Mozobil	United States	Serial	Serial 0520 to IND 55,851 for Mozobil; protocol amendment 004 to protocol AMD3100-CUP001, the compassionate use protocol	IND
775	29 Aug 2007	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; copies of Pre-NDA Briefing Document and CD containing Word document of questions	IND

776	29 Aug 2007	Mozobil	United States	Serial	Serial 0521 to IND 55,851 for Mozobil; pre-NDA briefing package	IND
777	30 Aug 2007	Mozobil	United States	Serial	Serial 0522 to IND 55,851 for Mozobil; letter of authorization	IND
778	04 Sep 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; FDA comments on Protocol MOZ00207	IND
779	05 Sep 2007	Mozobil	United States	Serial	Serial 0523 to IND 55,851 for Mozobil; IND safety report for protocol AMD3100-CUP001 MOZO-10476	IND
780	07 Sep 2007	Mozobil	United States	Serial	Serial 0524 to IND 55,851 for Mozobil; amendment to pre-NDA briefing package	IND
781	07 Sep 2007	Mozobil	United States	Annual Report	Annual Report for Mozobil ODD 03-1679 covering the reporting period 10 Sep 2006 through 7 Sep 2007	ODD
782	07 Sep 2007	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; a copy of the questions contained in serial 0524, an amendment to pre-NDA package	IND
783	12 Sep 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; FDA review of serial 0520 - amendment 004 to protocol AMD3100-CUP001	IND
784	14 Sep 2007	Mozobil	United States	Serial	Serial 0525 to IND 55,851 for Mozobil; protocol amendment 01 to Protocol MOZ00207	IND
785	17 Sep 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; FDA's preliminary responses to Genzyme's pre-NDA questions	IND
786	21 Sep 2007	Mozobil	United States	Serial	Serial 0526 to IND 55,851 for Mozobil; IND safety report	IND
787	21 Sep 2007	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; Genzyme requests clarification of FDA pre-NDA responses	IND
788	25 Sep 2007	Mozobil	United States	Serial	Serial 0527 to IND 55,851 for Mozobil; IND safety report follow-up 1 to AMD3100-CUP001/MOZO-10476	IND
789	27 Sep 2007	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; slides for pre-NDA meeting scheduled for 1 Oct 2007	IND
790	03 Oct 2007	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; Genzyme's draft version of pre-NDA meeting minutes from meeting of 1 Oct 2007 and request for comments on serial 0525	IND
791	05 Oct 2007	Mozobil	United States	Serial	Serial 0528 to IND 55,851 for Mozobil; IND safety report follow-up 2 to AMD3100-CUP001/MOZO-10476	IND
792	05 Oct 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil, FDA's official minutes of the 1 Oct 2007 pre-NDA meeting	IND
793	09 Oct 2007	Mozobil	United States	Serial	Serial 0529 to IND 55,851 for Mozobil; proposal	IND
794	12 Oct 2007	Mozobil	United States	Serial	Serial 0530 to IND 55,851 for Mozobil; initial 15-day IND safety report - AMD3100-CUP001/MOZO-10701	IND
795	15 Oct 2007	Mozobil	United States	Serial	Serial 0531 to IND 55,851 for Mozobil; protocol amendment 2 to Protocol AMD3100-2112	IND
796	16 Oct 2007	Mozobil	United States	Serial	Serial 0532 to IND 55,851 for Mozobil; IND safety report follow-up 3 to AMD3100-CUP001/MOZO-10476	IND

797	18 Oct 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil, FDA's reply to serial 0525	IND
798	24 Oct 2007	Mozobil	United States	Serial	Serial 0533 to IND 55,851 for Mozobil; IND safety report follow-up 1 to AMD3100-CUP001/MOZO-10701	IND
799	25 Oct 2007	Mozobil	United States	Serial	Serial 0534 to IND 55,851 for Mozobil; letter of authorization	IND
800	26 Oct 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; response to Genzyme's request for FDA update	IND
801	05 Nov 2007	Mozobil	United States	Serial	Serial 0535 to IND 55,851 for Mozobil; IND safety report follow-up 4 to AMD3100-CUP001/MOZO-10476	IND
802	05 Nov 2007	Mozobil	United States	Serial	Serial 0536 to IND 55,851 for Mozobil; submission of a new protocol, MOZ00707	IND
803	12 Nov 2007	Mozobil	United States	Serial	Serial 0537 to IND 55,851 for Mozobil, Amendment 1 to Protocol MOZ00207	IND
804	13 Nov 2007	Mozobil	United States	Serial	Serial 0538 to IND 55,851 for Mozobil; letter of authorization	IND
805	13 Nov 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 and NDA 022-311 for Mozobil; response to Genzyme's proposal	IND, NDA
806	14 Nov 2007	Mozobil	United States	Serial	Serial 0539 to IND 55,851 for Mozobil, Information Amendment: Pharmacology/Toxicology	IND
807	14 Nov 2007	Mozobil	United States	Contact Report	Sherwin Sattarzadeh of Genzyme contacted Chisa Byrd of FDA's Central Document Room on 14 Nov 2007 to request an NDA number of the upcoming Mozobil NDA; Ms. Byrd called back and reported that the number will be [NDA 022-311]	NDA
808	20 Nov 2007	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; approval of serial 0529, which was sent on 9 Oct 2007 (document ID 42751)	IND
809	14 Dec 2007	Mozobil	United States	Serial	Serial 0540 to IND 55,851 for Mozobil; letter of authorization	IND
810	19 Dec 2007	Mozobil	United States	Correspondence Sent	Correspondence to Mozobil IND 55,851; response to FDA's request for Clinical Pharmacology Highlights and latest investigator brochure (IB)	IND
811	07 Jan 2008	Mozobil	United States	Serial	Serial 0541 to IND 55,851 for Mozobil; letter of authorization	IND
812	07 Jan 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 of Mozobil, FDA comments	IND
813	08 Jan 2008	Mozobil	United States	Serial	Serial 0542 to IND 55,851 for Mozobil; letter of authorization	IND

814	11 Jan 2008	Mozobil	United States	Serial	Serial 0543 to IND 55,851 for Mozobil; letter of authorization	IND
815	18 Jan 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; FDA response to Genzyme's follow-up question	IND
816	20 Jan 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; FDA response to Genzyme's question	IND
817	23 Jan 2008	Mozobil	United States	Serial	Serial 0544 to IND 55851 for Mozobil, a copy of Pediatric Investigational Plan (PIP) Proposal that was sent to the EMEA	IND
818	15 Feb 2008	Mozobil	United States	Serial	Serial 0545 to IND 55,851 for Mozobil; letter of authorization	IND
819	19 Feb 2008	Mozobil	United States	Serial	Serial 0546 for IND 55,851 for Mozobil, New Protocol, number MOZ00607	IND
820	28 Feb 2008	Mozobil	United States	Serial	Serial 0547, IND Safety Report Initial 15-day Report MOZO-1000019 to IND 55,851 for Mozobil; patient was being treated under Protocol AMD3100-CUP001	IND
821	03 Mar 2008	Mozobil	United States	Serial	Serial 0548 to IND 55,851 for Mozobil; Protocol Amendment, Amendment 1 to MOZ00707	IND
822	20 Mar 2008	Mozobil	United States	Serial	Serial 0549, IND Safety Report, follow-up 1 to MOZO-1000019 to IND 55,851 for Mozobil;	IND
823	26 Mar 2008	Mozobil	United States	Serial	Serial 0550 to IND 55,851 for Mozobil, revised investigator's brochure	IND
824	27 Mar 2008	Mozobil	United States	Serial	Serial 0551 to IND 55,851 for Mozobil; letter of authorization	IND
825	27 Mar 2008	Mozobil	United States	Serial	Serial 0552, IND Safety Report, follow-up 2 to MOZO-1000019 to IND 55,851 for Mozobil;	IND
826	03 Apr 2008	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; response to FDA's request	IND
827	03 Apr 2008	Mozobil	United States	Contact Report	On 3 Apr 2008 representatives of Genzyme and FDA met via teleconference	IND
828	09 Apr 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; request for a copy of the Mozobil clinical investigator's brochure	IND

829	09 Apr 2008	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; in response to FDA's question from the teleconference of 3 Apr 2008,	IND
830	10 Apr 2008	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil;	IND
831	10 Apr 2008	Mozobil	United States	Contact Report	On 10 Apr 2008, Alice Kacuba of FDA called Sherwin Sattarzadeh to introduce herself as the new FDA project manager and to inform Genzyme that Dotti Pease the previous project manager for Mozobil, had retired	IND
832	15 Apr 2008	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; CMC follow up request	IND
833	15 Apr 2008	Mozobil	United States	Contact Report	On 15 Apr 2008 Sherwin Sattarzadeh of Genzyme called Carl Huntley of FDA seeking clarification on an email message	IND
834	15 Apr 2008	Mozobil	United States	Serial	Serial 0553 to IND 55,851 for Mozobil; 2 IND safety reports: follow-up 5 to AMD3100-CUP001/MOZO-10476 and follow-up 2 to AMD3100-CUP001/MOZO-10701	IND
835	15 Apr 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; FDA Request	IND
836	16 Apr 2008	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; clinical pharmacology highlights table and the IRB approved informed consent	IND
837	18 Apr 2008	Mozobil	United States	Serial	Serial 0554 to IND 55,851 for Mozobil; Protocol Amendment - New Investigator for Protocol MOZ00707	IND
838	24 Apr 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; approval letter for the EAP - extended access program	IND
839	24 Apr 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; review status of the EAP [extended access program] protocol [Protocol MOZ00607]	IND
840	29 Apr 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; notice that the approval letter of 24 Apr 2008 for the EAP - extended access program, has a typographical error in the header of the second page	IND
841	01 May 2008	Mozobil	United States	Serial	Serial 0555 to IND 55,851 for Mozobil; IND safety initial 15-day Report MOZO-1000040 from Protocol AMD3100-EU23	IND
842	05 May 2008	Mozobil	United States	Serial	Serial 0556 for IND 55,851 for Mozobil, request for Telecon meeting with FDA to discuss day 120 Safety Update Report (SUR)	IND

843	06 May 2008	Mozobil	United States	Serial	Serial 0557 to IND 55,851 for Mozobil; letter of authorization	IND
844	06 May 2008	Mozobil	United States	Serial	Serial 0558 to IND 55,851 for Mozobil; IND safety reports follow-up 6 to AMD3100-CUP001/MOZO-10476	IND
845	07 May 2008	Mozobil	United States	Serial	Serial 0559 to IND 55,851 for Mozobil; letter of authorization	IND
846	07 May 2008	Mozobil	United States	Serial	Serial 0560 to IND 55,851 for Mozobil; letter of authorization	IND
847	09 May 2008	Mozobil	United States	Contact Report	On 9 May 2008, Alice Kacuba of FDA called Sherwin Sattarzadeh with questions	IND
848	09 May 2008	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil, update by Genzyme of Protocol MOZ00607, the Extended Access Protocol, and a copy of serial 0556	IND
849	14 May 2008	Mozobil	United States	Contact Report	Two email contacts between Kathleen Greene of Genzyme and Ginny Ventura of FDA-CDER's Office of Business Process Support, on 14 May and 15 May 2008	NDA
850	15 May 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851, FDA will allow the electronic submission [eSub] of the dataset	IND
851	20 May 2008	Mozobil	United States	Serial	Serial 0561 to IND 55,851 for Mozobil; letter of authorization	IND
852	20 May 2008	Mozobil	United States	Serial	Serial 0562 to IND 55,851 for Mozobil; letter of authorization	IND
853	20 May 2008	Mozobil	United States	Serial	Serial 0563 to IND 55,851 for Mozobil; letter of authorization	IND
854	27 May 2008	Mozobil	United States	Serial	Serial 0564 to IND 55,851 for Mozobil; IND Safety Report Follow-up Report 1 to MOZO-1000040 from Protocol AMD3100-EU23	IND
855	28 May 2008	Mozobil	United States	Serial	Serial 0565 to IND 55,851 for Mozobil; letter of authorization f	IND
856	28 May 2008	Mozobil	United States	Serial	Serial 0566 to IND 55,851 for Mozobil; letter of authorization	IND
857	05 Jun 2008	Mozobil	United States	Correspondence Received	Correspondence to IND 55,851 for Mozobil; request for information about EAP - the extended access program	IND
858	06 Jun 2008	Mozobil	United States	Serial	Serial 0567 to IND 55,851 for Mozobil; letter of authorization	IND
859	12 Jun 2008	Mozobil	United States	Serial	Serial 0568 to IND 55,851 for Mozobil; response to FDA request	IND
860	12 Jun 2008	Mozobil	United States	Contact Report	On 12 Jun 2008 Alice Kacuba of FDA returned a call to Sherwin Sattarzadeh regarding the planned-for filing date of the NDA	IND, NDA

861	16 Jun 2008	Mozobil	United States	Application	Initial Application, Sequence 0000, to NDA 022-311 for Mozobil (plerixafor injection)	NDA
862	17 Jun 2008	Mozobil	United States	Serial	Serial 0569 to IND 55,851 for Mozobil; letter of authorization	IND
863	17 Jun 2008	Mozobil	United States	Serial	Serial 0570 to IND 55,851 for Mozobil, Amendment 1, protocol amendment: change in protocol, to protocol MOZ00607	IND
864	01 Jul 2008	Mozobil	United States	Serial	Serial 0571 to IND 55,851 for Mozobil, Annual Report covering the period 6 May 2007 through 5 May 2008	IND
865	02 Jul 2008	Mozobil	United States	Serial	Serial 0572 to IND 55,851 for Mozobil; letter of authorization	IND
866	02 Jul 2008	Mozobil	United States	Serial	Serial 0573 to IND 55,851 for Mozobil; letter of authorization	IND
867	09 Jul 2008	Mozobil	United States	Serial	Serial 0574 to IND 55,851 for Mozobil; letter of authorization	IND
868	09 Jul 2008	Mozobil	United States	Serial	Serial 0575 to IND 55,851 for Mozobil; Protocol Amendment - New Investigator for Protocol AMD3100-2112	IND
869	18 Jul 2008	Mozobil	United States	Contact Report	On 18 Jul 2008, Susan Jenney of FDA called Laura Mondano of Genzyme to introduce herself as the new Regulatory Project Manager assigned to NDA 022-311 for Mozobil	NDA
870	18 Jul 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil, acknowledgement of receipt of application [document ID 47669] sent and received on 16 Jun 2008	NDA
871	21 Jul 2008	Mozobil	United States	Contact Report	On 21 Jul 2008, Laura Mondano of Genzyme sent email to Susan Jenney of FDA confirming that the Genzyme Mozobil team is planning to attend an FDA meeting scheduled for Tuesday, 5 Aug	NDA
872	21 Jul 2008	Mozobil	United States	Clinical Trial Posting--Posted	Mozobil, MOZ00607, ClinicalTrials.gov, Registration Receipt	IND
873	22 Jul 2008	Mozobil	United States	Contact Report	On 22 Jul 2008, Susan Jenney of FDA emailed Laura Mondano of Genzyme requesting contact information	NDA
874	23 Jul 2008	Mozobil	United States	Contact Report	On 23 Jul 2008, Laura Mondano of Genzyme sent the contact information	NDA
875	25 Jul 2008	Mozobil	United States	Contact Report	On 25 Jul 2008, Laura Mondano of Genzyme called Susan Jenney of FDA	NDA
876	25 Jul 2008	Mozobil	United States	Contact Report	On 25 Jul 2008 Laura Mondano of Genzyme sent 3 separate email messages to Susan Jenney of FDA	NDA
877	01 Aug 2008	Mozobil	United States	Serial	Serial 0576 to IND 55,851 for Mozobil; letter of authorization	IND

878	01 Aug 2008	Mozobil	United States	Serial	Serial 0577 to IND 55,851 for Mozobil; letter of authorization	IND
879	01 Aug 2008	Mozobil	United States	Serial	Serial 0578 to IND 55,851 for Mozobil; letter of authorization	IND
880	01 Aug 2008	Mozobil	United States	Serial	Serial 0579 to IND 55,851 for Mozobil; letter of authorization	IND
881	01 Aug 2008	Mozobil	United States	Contact Report	On 1 Aug 2008, Sherwin Sattarzadeh of Genzyme responded to an email message from Alice Kacuba of FDA	NDA
882	01 Aug 2008	Mozobil	United States	Correspondence Sent	Correspondence to NDA 022-311 for Mozobil, slide set for NDA post submission meeting of 5 Aug 2008	NDA
883	06 Aug 2008	Mozobil	United States	Contact Report	On 6 Aug 2008, Susan Jenney of FDA emailed a list of FDA attendees of the 5 Aug 2008 Post Submission meeting for NDA 022-311 for Mozobil to Sherwin Sattarzadeh of Genzyme	NDA
884	08 Aug 2008	Mozobil	United States	Contact Report	On 7 Aug 2008, Susan Jenney of FDA called Laura Mondano of Genzyme requesting the location of the NDA Field Copy Certification, and on 8 Aug 2008, Sherwin Sattarzadeh of Genzyme returned the call	NDA
885	12 Aug 2008	Mozobil	United States	Serial	Serial 0580 to IND 55,851 for Mozobil; Protocol Amendment number 2 to protocol MOZ00207	IND
886	12 Aug 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil, Priority Review Designation Letter	NDA
887	13 Aug 2008	Mozobil	United States	Correspondence Sent	Correspondence sent to FDA regarding NDA 022-311 for Mozobil; sequence 0001, general correspondence, meeting minutes of the NDA post-submission meeting 5 Aug 2008	NDA
888	14 Aug 2008	Mozobil	United States	Serial	Serial 0581 to IND 55,851 for Mozobil; letter of authorization	IND
889	22 Aug 2008	Mozobil	United States	Contact Report	On 22 Aug 2008, Robert Young of FDA called Sherwin Sattarzadeh of Genzyme	NDA
890	26 Aug 2008	Mozobil	United States	Contact Report	On 26 Aug 2008, Sherwin Sattarzadeh of Genzyme emailed Robert Young of FDA	NDA
891	26 Aug 2008	Mozobil	United States	Serial	Serial 0582 to IND 55,851 for Mozobil; letter of authorization	IND
892	26 Aug 2008	Mozobil	United States	Serial	Serial 0583 to IND 55,851 for Mozobil; letter of authorization	IND
893	26 Aug 2008	Mozobil	United States	Correspondence Sent	Correspondence to NDA 022-311 for Mozobil,	NDA
894	26 Aug 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil; Sequence 0002, AMD3100-3101 and AMD3100-3102 Final 12-Month Graft Durability Reports	NDA

895	28 Aug 2008	Mozobil	United States	Serial	Serial 0584 to IND 55,851 for Mozobil; Protocol Amendment - New Investigator for Protocol MOZ00207	IND
896	28 Aug 2008	Mozobil	United States	Serial	Serial 0585 to IND 55,851 for Mozobil; letter of authorization	IND
897	28 Aug 2008	Mozobil	United States	Serial	Serial 0586 to IND 55,851 for Mozobil; letter of authorization	IND
898	29 Aug 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil, NDA filing review letter	NDA
899	04 Sep 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil (plerixafor injection); Sequence 0003, Response to Filing Communication Letter of 29 Aug 2008	NDA
900	05 Sep 2008	Mozobil	United States	Serial	Serial 0587 to IND 55,851 for Mozobil; IND Safety Report - Initial Report MOZO-1000038 for a patient participating in Protocol AMD3100-CUP001	IND
901	05 Sep 2008	Mozobil	United States	Serial	Serial 0588 to IND 55,851 for Mozobil; letter of authorization	IND
902	05 Sep 2008	Mozobil	United States	Annual Report	Annual Report for Mozobil ODD 03-1679 covering the reporting period 8 Sep 2007 through 5 Sep 2008	ODD
903	12 Sep 2008	Mozobil	United States	Serial	Serial 0589 to IND 55,851 for Mozobil; letter of authorization	IND
904	12 Sep 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil, clinical pharmacology information request	NDA
905	15 Sep 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil (plerixafor injection); Sequence 0004, response to request for information of 12 Sep 2008	NDA
906	15 Sep 2008	Mozobil	United States	Contact Report	On 15 Sep 2008, Sherwin Sattarzadeh of Genzyme responded to a request from Susan Jenney of FDA for an information request	NDA
907	19 Sep 2008	Mozobil	United States	Contact Report	On 19 Sep 2008, Lloyd Johnson of FDA returned a call to Sherwin Sattarzadeh of Genzyme	IND
908	23 Sep 2008	Mozobil	United States	Correspondence Sent	Correspondence to IND 55,851 for Mozobil; request that FDA acknowledge receipt of serial 0544, sent on 23 Jan 2008	IND
909	24 Sep 2008	Mozobil	United States	Serial	Serial 0590 to IND 55,851 for Mozobil; letter of authorization	IND
910	01 Oct 2008	Mozobil	United States	Serial	Serial 0591 to IND 55,851 for Mozobil; IND safety reports follow-up 1 to MOZO-1000038 for a patient participating in Protocol AMD3100-CUP001	IND
911	02 Oct 2008	Mozobil	United States	Correspondence Sent	Correspondence to NDA 022-311 for Mozobil, Genzyme's authorizes FDA to send CMC information request by email	NDA
912	02 Oct 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil, email copy of FDA information request letter regarding CMC issues	NDA
913	02 Oct 2008	Mozobil	United States	Correspondence Sent	Correspondence to NDA 022-311 for Mozobil, receipt confirmation of FDA information request letter	NDA
914	02 Oct 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil, FDA information request letter	NDA

915	03 Oct 2008	Mozobil	United States	Serial	Serial 0592 to IND 55,851 for Mozobil; letter of authorization	IND
916	08 Oct 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil, FDA clinical pharmacology findings.	NDA
917	08 Oct 2008	Mozobil	United States	Correspondence Sent	Correspondence to NDA 022-311 for Mozobil, Genzyme's acknowledgement of FDA's clinical pharmacology findings	NDA
918	15 Oct 2008	Mozobil	United States	Contact Report	On 15 Oct 2008, Deborah Mesmer of FDA called Laura Mondano of Genzyme called about pre-submission and pre-approval communications regarding NDA 022-311 for Mozobil, resulting in a later call by Bem Atsma of Genzyme to Ms. Mesmer	NDA
919	15 Oct 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil (plerixafor injection); Sequence 0005, 4 month (120 day) safety update report	NDA
920	21 Oct 2008	Mozobil	United States	Amendment	Efficacy information amendment, sequence 0006 to NDA 022-311 for Mozobil, response to FDA letter of 8 Oct 2008, request for information [document ID 49736] regarding clinical pharmacology	NDA
921	21 Oct 2008	Mozobil	United States	Serial	Serial 0593 to IND 55,851 for Mozobil; protocol amendment to 2 clinical trials: AMD3100-3101-LTF and AMD3100-3102-LTF	IND
922	22 Oct 2008	Mozobil, Renvela	United States	Contact Report	On 22 Oct 2008, Jose Hernandez of FDA called Alicia Jeannotte of Genzyme regarding planned-for GMP inspections	NDA
923	22 Oct 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil; clinical pharmacology information request involving pharmacokinetics for some subjects enrolled in protocol AMD3100-1101	NDA
924	24 Oct 2008	Mozobil	United States	Serial	0594 - IND Cross Reference letter	IND
925	27 Oct 2008	Mozobil	United States	Serial	Serial 0595 to IND 55,851 for Mozobil; letter of authorization	IND
926	27 Oct 2008	Mozobil	United States	Correspondence Sent	Correspondence to NDA 022-311 for Mozobil; response to FDA clinical pharmacology information request involving pharmacokinetics for some subjects enrolled in protocol AMD3100-1101 of 22 Oct 2008	NDA
927	27 Oct 2008	Mozobil	United States	Contact Report	On 27 Oct 2008, Susan Jenney of FDA called Laura Mondano of Genzyme to schedule a teleconference meeting with the FDA Clinical Pharmacology review team for Friday, 31 Oct 2008, at 9:30 a.m.	NDA
928	28 Oct 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil (plerixafor injection); Sequence 0007, response to FDA information request dated 22 Oct 2008 [document ID 49993]	NDA
929	29 Oct 2008	Mozobil	United States	Serial	Serial 0596 to IND 55,851 for Mozobil; letter of authorization	IND

930	30 Oct 2008	Mozobil	United States	Correspondence Received	Corresponddence to NDA 022-311 for Mozobil; FDA information request on carton and vial label	NDA
931	31 Oct 2008	Mozobil	United States	Memo to File	This is to document the background, summary, and conclusions from a Oct 31, 2008 teleconference with FDA.	NDA
933	03 Nov 2008	Mozobil	United States	Contact Report	On 3 Nov 2008, via email, Denise Oliveira of Genzyme asked Lonnie Smith of FDA	NDA
934	03 Nov 2008	Mozobil	United States	Correspondence Sent	Correspondence to NDA 022-311 for Mozobil; question for FDA statistician	NDA
935	03 Nov 2008	Mozobil	United States	Contact Report	On 3 Nov 2008, Laura Mondano of Genzyme called Susan Jenney of FDA regarding an amendment to NDA 022-311	NDA
936	04 Nov 2008	Mozobil	United States	Serial	Serial 0597 to IND 55,851 for Mozobil; IND Safety Report, Initial Report MOZO1000112 for Mozobil	IND
937	05 Nov 2008	Mozobil	United States	Serial	Serial 0598 to IND 55,851 for Mozobil - Protocol Amendment - New Investigator for Protocol MOZ00207	IND
938	06 Nov 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil; CMC information request	NDA
939	07 Nov 2008	Mozobil	United States	Contact Report	On 7 Nov 2008, Laura Mondano of Genzyme responded to an email message from Deborah Mesmer of FDA regarding the status of Genzyme's response to FDA's 6 Nov CMC information request letter (document ID 50224)	NDA
940	07 Nov 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil; Sequence 0008; Information Amendment - update to safety information and revised draft labeling	NDA
941	11 Nov 2008	Mozobil	United States	Serial	Serial 0599 to IND 55,851 for Mozobil; IND Safety Report, Follow-up report 2 MOZO-1000038 for Mozobil; Protocol AMD3100-CUP001	IND
942	12 Nov 2008	Mozobil	United States	Serial	Serial 0600 to IND 55,851 for Mozobil, Letter of Authorization, IND Cross Reference Authorization for Protocol MOZ00607	IND
943	12 Nov 2008	Mozobil	United States	Contact Report	On 12 Nov 2008, Laura Mondano of Genzyme responded to a request from Robert Young of FDA, for AnorMED history and Genzyme's acquisition	NDA
944	12 Nov 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil; Sequence 0009; response to information and clarification requests dated 2 Oct 2008, 30 Oct 2008, and 5 Nov 2008	NDA
945	14 Nov 2008	Mozobil	United States	Serial	Serial 0601 to IND 55,851 for Mozobil, with reference to Sequence Number 0008 to NDA 022-311 for Mozobil, Information Amendment: New Safety Information	IND
946	14 Nov 2008	Mozobil	United States	Serial	Serial 0602 to IND 55,851 for Mozobil; Letter of Authorization	IND

947	14 Nov 2008	Mozobil	United States	Contact Report	Sherwin Sattarzadeh of Genzyme called Susan Jenney, FDA Project Manager for Mozobil and left a voicemail informing that an amendment will be sent to NDA on 14 Nov 2008	NDA
948	14 Nov 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil; Sequence 0010; Information Amendment	NDA
949	18 Nov 2008	Mozobil	United States	Contact Report	On 18 Nov 2008, Sherwin Sattarzadeh of Genzyme sent email to Susan Jenney of FDA regarding post marketing commitment number 3	NDA
950	19 Nov 2008	Mozobil	United States	Contact Report	On 19 Nov 2008, Sherwin Sattarzadeh of Genzyme responded to email from Susan Jenney of FDA	NDA
951	19 Nov 2008	Mozobil	United States	Correspondence Sent	Correspondence regarding the pre-approval inspection for Mozobil;	NDA
952	20 Nov 2008	Mozobil	United States	Serial	Serial 0603 to IND 55,851 for Mozobil; initial IND safety report MOZO-1000123 for a patient participating in Protocol MOZ00607	IND
953	20 Nov 2008	Mozobil	United States	Contact Report	On 20 Nov 2008, Susan Jenney of FDA responded to email from Sherwin Sattarzadeh of Genzyme regarding his inquiry	NDA
954	21 Nov 2008	Mozobil	United States	Contact Report	On 21 Nov 2008, Sherwin Sattarzadeh of Genzyme responded to email from Susan Jenney of FDA	NDA
955	21 Nov 2008	Mozobil	United States	Contact Report	On 21 Nov 2008, Sherwin Sattarzadeh of Genzyme responded to email from Susan Jenney of FDA	NDA
956	21 Nov 2008	Mozobil	United States	Contact Report	On 21 Nov 2008, Alice Kacuba of FDA called Sherwin Sattarzadeh of Genzyme to inquire about the status of Mozobil IND 55,851	IND
957	21 Nov 2008	Mozobil	United States	Serial	Serial 0604 to IND 55,851 for Mozobil; Letter of Authorization	IND
958	21 Nov 2008	Mozobil	United States	Amendment	Amendment to NDA 022-311 for Mozobil; Sequence 0011; Quality Information Amendment - Response to 6 Nov 2008 Information Request (document ID 50224)	NDA
959	21 Nov 2008	Mozobil	United States	Correspondence Received	FDA Comments on Draft US PI	NDA
960	21 Nov 2008	Mozobil	United States	Amendment	Quality Information Amendment, Sequence 0011, Response to FDA Information Request of 6 Nov 2008 (document ID 50224)	NDA

961	24 Nov 2008	Mozobil	United States	Correspondence Sent	Tumor Cell Mobilization White Paper and Request for Teleconference	NDA
962	26 Nov 2008	Mozobil	United States	Correspondence Sent	Genzyme's Response to FDA Comments on US PI	NDA
963	26 Nov 2008	Mozobil	United States	Amendment	2008-11-26 - Sequence 0012 - Quality Information Amendment - Response to 02 Oct 2008 - Information Request (Question 1a)	NDA
964	01 Dec 2008	Mozobil	United States	Correspondence Received	FDA Comments on Draft US PI	NDA
965	02 Dec 2008	Mozobil	United States	Correspondence Sent	Email to FDA with a preliminary response to 12/01/08 FDA labeling comments	NDA
966	02 Dec 2008	Mozobil	United States	Correspondence Sent	Response to FDA's comments on Draft US PI	NDA
967	02 Dec 2008	Mozobil	United States	Correspondence Sent	Confirmation on FDA's response	NDA
968	02 Dec 2008	Mozobil	United States	Serial	0605 - Information Amendment	IND
969	03 Dec 2008	Mozobil	United States	Amendment	2008-12-03 - Seq 0013 - Information Amendment - Revised Draft Labeling and Carton and Vial	NDA
970	04 Dec 2008	Mozobil	United States	Correspondence Sent	FDA Comments and Genzyme's Response on US PI	NDA
971	04 Dec 2008	Mozobil	United States	Correspondence Sent	Patient IDs for Phase 3 patients who did not receive study drug	NDA
972	05 Dec 2008	Mozobil	United States	Correspondence Received	FDA Request and Genzyme Response	NDA
973	05 Dec 2008	Mozobil	United States	Correspondence Received	FDA Comments on draft US PI and Carton/Vial Labels	NDA
974	05 Dec 2008	Mozobil	United States	Correspondence Sent	Response to FDA draft US PI comments	NDA
975	05 Dec 2008	Mozobil	United States	Serial	Serial 0606 to IND 55,851 for Mozobil; IND Safety Report Initial report 2 MOZO-1000128 for Mozobil; Protocol AMD3100-CUP001	IND
976	08 Dec 2008	Mozobil	United States	Amendment	2008-12-08 - Seq 0014 - Safety Information Amendment - Tumor Mobilization White Paper	NDA
977	08 Dec 2008	Mozobil	United States	Correspondence Sent	Acknowledgement to Submit TCM White Paper	NDA
978	09 Dec 2008	Mozobil	United States	Correspondence Received	FDA Request for PAI Inspection Status Update	NDA
979	09 Dec 2008	Mozobil	United States	Correspondence Sent	Revised Carton and Vial Labels per FDA Guidance (Arial font labels)	NDA
980	10 Dec 2008	Mozobil	United States	Correspondence Sent	Response to PAI Inspection Status Request	NDA
981	10 Dec 2008	Mozobil	United States	Correspondence Received	Mozobil Burst/Notice from Susan Lange at FDA	NDA
982	10 Dec 2008	Mozobil	United States	Correspondence Received	Revised Set of Post Marketing Commitments	NDA
983	11 Dec 2008	Mozobil	United States	Correspondence Sent	List of FDA and Genzyme 2008-12-10 Teleconference Attendees	NDA
984	11 Dec 2008	Mozobil	United States	Correspondence Sent	Genzyme's Response to PMCs	NDA
985	11 Dec 2008	Mozobil	United States	Correspondence Sent	Genzyme's Response to PMCs (Version 2)	NDA
986	11 Dec 2008	Mozobil	United States	Correspondence Sent	Genzyme's Response to PMCs (Version 3)	NDA
987	11 Dec 2008	Mozobil	United States	Correspondence Sent	Genzyme's Final US PI and Carton and Vial Labels	NDA
988	12 Dec 2008	Mozobil	United States	Correspondence Sent	Genzyme's Comments on FDA's Mozobil Burst	NDA
989	12 Dec 2008	Mozobil	United States	Correspondence Sent	Administrative Change to Final US PI	NDA

990	12 Dec 2008	Mozobil	United States	Correspondence Received	Additional Comments Received from FDA on the US PI	NDA
992	15 Dec 2008	Mozobil	United States	Amendment	Mozobil 2008-12-15 Information Amendment - Final Labeling Text	NDA
993	15 Dec 2008	Mozobil	United States	Amendment	Mozobil 2008-12-12 Information Amendment - Revised Draft Labeling Text - Sequence 0015	NDA
994	15 Dec 2008	Mozobil	United States	Correspondence Sent	Genzyme's Response to FDA's 12/12/2008 Labeling Comments	NDA
995	15 Dec 2008	Mozobil	United States	Correspondence Received	Correspondence to NDA 022-311 for Mozobil; approval letter to the NDA.	NDA

EXHIBIT F

In re patent of Gary J. Bridger et al.
USP 5,583,131
Approved Product: MOZOBIL™ (plerixafor)
Application for Patent Term Extension
Customer No. 22852

PATENT
Attorney Docket No. 20006 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the patent of: Gary J. Bridger, *et al.*	)	Approved Product: MOZOBIL™ (plerixafor)
Patent No.: 5,583,131	)	U.S. F.D.A. Approval Date: December 15, 2008
Granted: December 10, 1996	)	
Title: AROMATIC-LINKED POLYAMINE MACROCYCLIC COMPOUNDS WITH ANTI-HIV ACTIVITY	)	

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Attachment F

Sir:

CERTIFICATION

I, CHARLES E. VAN HORN, do hereby certify that this accompanying application for extension of the term of U.S. Patent No. 5,583,131 under 35 U.S.C. § 156 including its attachments and supporting papers is being submitted as one original and two (2) copies thereof, pursuant to 37 C.F.R. § 1.740(b).

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Date: 06 February 2009

By: Charles E Van Horn
Charles E. Van Horn
Reg. No. 40,266